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THE
LARYNGOSCOPE.

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DESENSITIZATION BY HISTAMINE (HISTAMINE AZOPROTEIN) IN VERTIGO, PERIODIC HEADACHES AND VASOMOTOR (ALLERGIC) RHINITIS. REVIEW OF THE LITERATURE AND REPORT OF 102 PERSONAL CASES.*

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In most respects otolaryngology is a very highly specialized branch of medicine. Like all other branches, however, it involves the treatment of certain obscure cases, the exact relationship of which to the specialty is not always clear, chiefly because there is no evident anatomic-pathologic basis for the symptomatology they present.

Something must be done for these unfortunate persons. At best, their symptoms interfere with their mode of life and incapacitate them at more or less frequent intervals. At worst, they make it impossible for them to earn their livelihood. That the group includes a certain number of persons who actually have nothing the matter with them is probably true, though the physician to whose lips the diagnosis of neurosis comes readily would do well to remember Lord Moynihan's caustic comment that under these circumstances neurosis often means "I don't know."

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It is always desirable to institute therapy on the basis of full knowledge of the pathologic process to be treated, but it is not always possible. If, therefore, therapy be in part empiric, there is always justification for the attempt if *1.* it is applied with such precautions that it does no harm, *2.* if it serves as a substitute for more radical measures, and *3.* if it relieves the patient, even if the relief must be evaluated by subjective and not by objective criteria. As Howard Kelly once understandingly remarked in another connection, what the patient seeks from the physician is relief, with or without a sound theory behind it.

Some *apologia* of this sort is necessary on the part of the otolaryngologist who proposes to present the therapy of so-called physical or intrinsic allergy as it relates to his specialty. Why he is chosen to treat the victims of this form of allergy is evident from what Williams[1] has chosen to call "the intrinsic allergy syndrome." Essentially it consists of *1.* vertigo, which may or may not take the form of true Ménière's disease, with associated tinnitus and deafness; *2.* periodic headache, which may or may not take the form of true migraine or of the "histaminic cephalgia" described by Horton;[2] *3.* vasomotor rhinitis; and *4.* cephalgic myalgia. All components of the syndrome appeared in four of the 372 cases studied by Williams, and the first three components appeared in three of the 102 cases reported herewith. Although I have observed cases of cephalic myalgia, personally I have not treated them by the method to be described in this communication.

THE NATURE OF ALLERGY.

While a complete discussion of allergy is obviously impossible within the limits of this paper, a brief outline of certain fundamental considerations is necessary before the presentation of either the therapeutic regimen or its results, for the reason that the concept of allergy as related to otolaryngology is still far from being generally realized. Piness and Miller[3] wrote in 1939 that they found themselves obliged to say all over again what they had said in 1925 concerning the allergic aspects of sinus disease in children, because there was still a

complete lack of appreciation of the frequency and the consequences of the condition. Richards,[4] in 1944, pointed out that until 1913 the *Transactions of the American Laryngological, Rhinological and Otolaryngological Society, Inc.*, contained no mention of the word allergy, which appeared in only four titles between 1921 and 1930, though in 18 between 1931 and 1944. Within the last few years the work of Hansel,[5] Farmer,[6] Williams,[1] Code[7] and numerous other workers has done much to lay down principles of diagnosis and to establish a rational approach to therapy.

Allergy can be briefly defined as an *individual* hypersensitivity to physical, chemical, biologic or psychic stimuli which do not provoke similar reactions in nonsensitive subjects. The causative agents are specific, and organs or systems are involved selectively. Finally, the reactions are entirely out of proportion to the apparent insignificance of the causative agents.

Experimental and clinical observations[8-14] over a long period of years have led to the assumption that anaphylactic shock and allergy are both caused by the release into the system of a substance which is now believed to be histamine.* When histamine, which exists pre-formed in the tissue cells as one of their normal constituents, is released upon the contact of a hypersensitive organism with specific causative stimuli, three major effects are the results: *1.* contraction of smooth muscle; *2.* dilatation and increased permeability of the capillaries, with the production of edema; *3.* increased secretion by the secretory glands.[7] Clinically the manifestations are modified by the organ or system in which the reaction occurs, which explains why one patient has asthma, another urticaria and a third, vasomotor (allergic) rhinitis.

THE HISTAMINE THERAPY OF ALLERGY.

If the (greatly simplified) explanation of allergy just outlined be accepted as correct, it would seem logical to undertake the treatment of allergic disease by desensitization

*Limitations of space do not permit the presentation of any proof of this assumption in the body of this communication. It is, however, presented briefly in an appendix (Appendix II), which may be read or disregarded as the reader may wish.

with histamine, exactly as desensitization with other agents is achieved. Theoretically the therapy of allergy is quite simple: one merely determines the causative allergen or allergens in the special case, and then either keeps the patient from contact with them or desensitizes him with them. In practice, however, as physicians and patient alike have learned to their sorrow, neither diagnosis nor therapy is quite so simple. In the first place, innumerable allergens have already been identified, and the chances are that innumerable others will be. As a result, the number of specific substances used for desensitization is already very large, and the therapy of the future promises to be even more complex than it is at present. In the second place, some patients are sensitive to multiple stimuli, and desensitization is correspondingly complicated. Finally, in numerous instances, although the allergic nature of the disease is apparent, the causative allergen (allergens) is never identified by any testing. The reduction of the present complex method of desensitization with numerous special agents, to desensitization with a single basic agent (histamine) would obviously solve many therapeutic problems, including the problem of the patient whose causative allergen has never been identified. The group of patients to be reported in this communication falls chiefly into the latter group.

Although histamine was not isolated from the human tissues until 1930, by Best and his associates,[15] it had been prepared synthetically by Windaus and Vogt in 1907, and seems to have been first used clinically by Ramirez and St. George,[16] in 1924. Their results in 10 patients with "endogenous asthma" were not encouraging. Occasional workers used or suggested the use of histamine therapy for various definitely or presumably allergic conditions in the intervening years,[17,18] but it was not until the later 'thirties that the method came into any sort of popularity, and even at the present time the number of physicians who employ it is still very limited.

Histaminase therapy would seem even more rational than histamine therapy, since histaminase, which was isolated by

Best and McHenry,[19] in 1927, has the property of inactivating histamine completely both in man and animals. Its physiologic effect has recently been clearly demonstrated by Roth and Horton[20] in a series of carefully controlled studies. Its therapeutic effects, however, have been almost uniformly poor.[21,22] It was not to be expected that they would be otherwise, since histaminase inactivates histamine very slowly, over a period of hours, while the release and action of histamine is a matter of minutes, if not of seconds.

Most of the cases of histamine desensitization now on record in the literature were treated with histamine diphosphate, an effective preparation, but, like all previous preparations, nonantigenic. To make histamine antigenic, it must be linked with some substance possessing antigenic properties. This was finally achieved by Fell, Marshall and Rodney[23,24] in the preparation of histamine azoprotein (hapamine), the ability of which to develop in animals and man some degree of immunity to histamine has been demonstrated[23-27] by various serologic and immunologic tests, as well as clinically.*

PERSONAL STUDIES WITH HISTAMINE AZOPROTEIN.

Histamine azoprotein first came to my attention in September, 1943, and to date (Sept. 1, 1945) I have used it in 142 cases of vertigo, periodic headache, allergic rhinitis, and dermatitis in or about the ear. Forty of these cases have been treated since Jan. 1, 1945, and are not included in this study because of the brevity of the possible period of observation.

Since the method of administration is practicaly the same in all conditions and agrees in general with the methods of others who have used this preparation, a general statement of the regimen of therapy can be made to cover all conditions.

The patient who comes to the office complaining of one or more of the symptoms listed is submitted to a complete physical examination, including, if indications exist, an examination of the central nervous system. A complete otolaryn-

*Because of limitations of space, the details of the development and testing of histamine azoprotein are presented in an appendix (Appendix III), which may be read or disregarded as the reader may wish.

gologic examination is then carried out, including a search for possible labyrinthine pathology. Routine laboratory tests are made and special tests, including the basal metabolic rate determination, are added as indicated.

Demonstrable pathologic conditions in the ears, nose or throat are treated by routine methods. If symptoms are not improved, allergic testing is done, and a fair trial is made of allergic therapy. If no relief is secured, histamine desensitization is begun, except in the cases of patients suffering from vertigo who are placed for five days on a modified Furstenberg[28] regimen (a sodium-free diet, with restricted fluids, following a dose of epsom salts — a tablespoonful of salt crystals in just enough water to dissolve them).

Patients whose condition warrants no delay, such as those suffering from disabling vertigo, are hospitalized and treated at once, without delay for time-consuming studies. The cautious administration of histamine, as Shea[29] has pointed out, does no harm, even if on further investigation the condition proves to be of nonallergic origin, and the prompt relief of a distressing symptom is justification for the procedure. These patients are usually treated intravenously.

Treatment in all patients except the group just mentioned begins with a subcutaneous injection of 0.05 cc. of azoprotein. The second dose is 0.1 cc., and each succeeding injection is increased by 0.1 cc. until a dosage of 1 cc. is reached. The injections are usually given on alternate days, unless symptoms are particularly distressing, when they are given daily, and in dermatitis cases, have been given twice daily. After the level of 1 cc. is reached, injections in this dosage are given weekly for four doses, and are followed by maintenance doses of 0.5 cc. weekly for eight weeks.

The usual patient receives a total of 9.55 cc. of histamine azoprotein over a period of approximately 13 weeks. In the occasional case a larger dose over a longer period of time is required, and in a few instances maintenance doses have been taken for a year or more. In a few cases results have been so prompt that treatment was discontinued short of the usual

levels; in a number of instances the patients discontinued treatment, against advice, at much earlier periods because they regarded themselves as cured. In these circumstances some have relapsed, but some have remained well to date.

The literature suggests that the majority of observers have followed substantially the dosage just described. Cohen,[25] however, gives an initial dose of 0.1 cc., a second dose of 0.5 cc., and five 1 cc. doses at five-day intervals, followed, after a rest period of two months, by four injections on a similar stepped-up schedule. In view of the numerous, though insignificant, reactions I have had with much smaller and more cautiously given injections, I should be reluctant to use dosages in this amount.

All patients treated with histamine azoprotein, without exception, are required to remain in the office under observation for a minimum of 20 minutes after each injection. During this time a syringe of epinephrine, the specific physiologic antagonist to histamine, is kept at hand, although only occasionally has it been necessary to use it.

In this series of 102 cases, reactions were insignificant in all but one or two cases. One patient, however, discontinued treatment because of a severe reaction, and one or two others hesitated for several days before permitting a second injection. Whenever a reaction occurred, the dosage was reduced to the dosage given at the injection previous to the reaction and was gradually stepped up again. Sometimes, as an additional precaution, several injections were given at the same level before the amount was again increased. The policy in all cases, in short, was a gradual increase of an originally minimum dose, with absolute individualization of each patient.

Reactions. all of which, however minimal, are listed in Table 1, chiefly took the form of local manifestations. Not only the site of the most recent injection but the sites of all previous injections reacted similarly. A few reactions took the form of asthmatic attacks, even in patients not previously subject to asthma, or of transient aggravation of vertigo,

headache or rhinitis, as the case might be. It was occasionally observed that in some cases, in which the previous response had been slow or imperceptible, improvement after the reaction was rapid and striking.

TABLE 1. REACTIONS (ALL) IN 102 CASES OF VARIOUS FORMS OF ALLERGY TREATED BY HISTAMINE AZOPROTEIN.

Case No.	No. of Injection	*Amount Injected	*Total Dosage	Type Reaction
		VERTIGO.		
6	8th	0.7	2.85	Local
8	5th	0.4	1.85	Local, increase of vertigo
10	8th	0.7	2.85	Local
11	5th	0.4	1.05	Local, increase of vertigo
18	4th	0.3	0.65	Local
20	8th	0.7	2.85	Local, increase of vertigo
21	4th	0.3	0.65	Asthmatic
22	5th	0.4	1.05	Increased vertigo, headache, nausea
25	5th	0.4	1.05	Local
26	8th	0.7	2.85	Asthmatic. Patient refused further treatment
27	5th	0.4	1.05	Asthmatic
28	4th	0.3	0.65	Local
30	11th	1.0	5.55	Asthmatic. This patient had previously had intravenous therapy
		ALLERGIC RHINITIS.		
6	8th	0.7	2.85	Local, severe
9	3rd	0.2	0.35	Asthmatic
13	†1st	0.5	.....	Asthmatic
14	5th	0 4	1.05	Local
20	8th	0.7	2.85	Local
22	†1st	0.5	.....	Asthmatic
24	5th	0.4	1.05	Asthmatic
28	8th	0.7	2.85	Local
		DERMATITIS.		
7	8th	0.7	2.85	Local
8	4th	0.3	0.65	Asthmatic
10	3rd	0.2	0.35	Local

*In cc.
†Second series, following recurrence of symptoms.

It might be well to emphasize that the rise in gastric acidity, which was one of the objections to the preparations of histamine previously used, and which actually caused ulceration in one reported case,[30] does not occur with histamine azoprotein. Sheldon and his associates[27] found no rise of gastric acidity following treatment with hapamine in patients

who had previously shown a marked rise after the injection of 0.03 mg. of histamine. No patient in my own series suffered any gastric symptoms following injections.

The reports which follow are necessarily recorded statistically and in very brief form. They should be interpreted, however, in the light of the relief secured for patients who, in many instances, had had no relief from numerous other treatments, many of them much more drastic, and who in most instances were seriously inconvenienced if not actually disabled by their illnesses.

VERTIGO.

Shea[29] has estimated that vertigo is the chief complaint of possibly 10 per cent of all patients who consult the otolaryngologist for chronic conditions. In the pure form, that is, in the syndrome consisting of sudden recurrent attacks associated with tinnitus and deafness (Ménière's disease), vertigo is relatively infrequent but fearfully disabling. My own experience parallels that of many others, that the disease may begin with a single symptom, usually vertigo, and that deafness is evidence of advanced Disease. My own experience, again, parallels Horton's:[31] If the patient can be treated while vertigo is the only symptom, deafness can be prevented in a large number of cases.

The histamine therapy of vertigo is based on the concept that Ménière's disease is the result of a local edematous process involving the labyrinth, the process itself being the result of local alterations in the permeability of the capillary wall. When deafness is the predominant symptom, the essential pathologic process is probably in the cochlea. I have not been able to confirm or to accept Atkinson's[32] concept that Ménière's disease (as well as migraine) has a dual etiology, a small group being caused by primary vasodilatation, the result of sensitivity to histamine, and a larger group caused by primary vasoconstriction. As Horton[31] has remarked, the problem is not so simple from the standpoint of either diagnosis or treatment.

Horton[33] first unwittingly treated Ménière's disease with histamine; while desensitizing a patient with histaminic cephalgia, he found that he had also relieved his daily vertigo and tinnitus. After he had relieved three other patients by subcutaneous injections, he learned of Alexander and Elliott's[34] results in chronic urticaria by intravenous injections of histamine, and switched to this method. The first patient, who had been bedridden for three weeks, literally took up his bed and walked immediately after treatment. In 1941, Horton reported that to date he had treated 49 patients by this method, 25 of whom had previously been treated by the Furstenberg method with only transient results, if any benefit at all. All were promptly relieved of vertigo, though the relief of tinnitus and auditory impairment was less striking. Rainey,[35] Shea,[29,36] Rubenstein,[37] Ingham[38] and Turvey,[39] among others, have reported generally good and frequently dramatic results from histamine desensitization in pure Ménière's disease or vertigo. Atkinson[32] considers the method contraindicated if not actually harmful in his so-called vasoconstrictor group, which constitutes 75 per cent of all such patients.

Over the 16-month period ending Jan. 1, 1945, I treated 40 patients with vertigo in the form of pure Ménière's disease or in the incomplete form, by histamine azoprotein. Nineteen were men and 21 women. The age range was from 13 years (in two cases) to 71 years and the great majority of patients was over 35 years of age.

In seven instances the vertigo was extremely acute; five patients could not sit up or turn their heads on the pillow. In 22 cases the vertigo was positional or was greatly aggravated by changes of position. The duration ranged from a few days to 15 years. Two patients had a family history of allergy, and two had children who suffered from migraine or had had asthma in childhood. Previous treatment, with transient if any relief, had included treatment directed toward the biliary tract and the liver, change of glasses, sedatives of various kinds, various otolaryngologic methods, including hay fever. One patient had a history of colitis, and another

several sinus operations in one case, and various allergic methods. One patient had been treated by nicotinic acid, and another by histamine diphosphate, which had to be discontinued because of tachycardia.

It is of interest that five patients with vertigo also suffered from periodic rhinitis, three from vasomotor rhinitis, and two from both conditions. In eight instances, in two of which polypi were present, the nasal mucosa was pale, boggy and entirely typical of allergic rhinitis. Other positive physical findings consisted of sphenoid sinus disease; immature cataracts; the carotid sinus syndrome; and, in seven cases, occlusion of the Eustachian tubes. Three patients who had not complained of impairment of hearing were found to have considerable impairment on audiometric testing. Inflation of the Eustachian tubes, which was carried out before therapy in all cases, increased the vertigo in three instances, in one instance being associated with nausea and in another with nystagmus.

Two of the patients suffering from acute vertigo were removed to the hospital and treated intravenously with histamine diphosphate (1 cc. in 250 cc. of physiologic salt solution at the rate of 60 drops per minute over a minimum period of 90 minutes); relief was immediate. Subcutaneous therapy was then carried out with histamine azoprotein according to the method described.

The duration of active therapy ranged from three weeks in one patient (who had a severe asthmatic reaction and declined to continue treatment) to 17 weeks in another. The majority was treated between nine and 11 weeks. Four, however, were treated for less than a month, because results were so prompt that discontinuation of treatment was regarded as safe and has so proven.

Two patients had recurrences at seven weeks and at 13 months; in the former case, treatment had been discontinued against advice. Both were relieved by a repetition of treatment. Four patients continued maintenance doses of 0.5 cc. for periods ranging from 14 to 40 weeks, and a fourth has

taken 1 cc. per week for 44 weeks. With the exceptions noted, the results were good in all cases over the period of observation, which ranged from four to six months in four cases, and from six to 22 months in the remaining cases; 15 patients have been followed for more than a year.

Illustrative case reports are appended (Appendix I).

PERIODIC HEADACHE.

The evidence for the allergic basis of period headache[40-49] is too extensive to be repeated here and is still incomplete.* Migraine, like vertigo, does not always appear in its complete form, nor is the allergic origin always possible to demonstrate. As Derbes and his co-authors[50] point out, skin tests, which are useful in identifying inhalant allergens, leave much to be desired in identifying dietary offenders, and are equally unsatisfactory, it should be noted, in identifying other varieties.

The list of remedies suggested for periodic headaches makes clear the necessity for better therapeutic methods. Some of them are entirely empirical, some of them are not free from risk, and most of them are unsatisfactory from the standpoint of end-results. Patzer and Engelhardt,[51] who had good results with periarterial infiltration with eucupine and novocaine, point out the usefulness of this method from the diagnostic standpoint: it demonstrates that arterial vasodilatation is (or is not) the cause of the headache. Atkinson[32] reports good results with nicotinic acid, but my own results with it were poor, and the patients objected to the flushing and other symptoms which followed even small doses. Reconstruction of the mode of life is an obvious mode of treatment, particularly for patients on the intellectual level, who are likely to live in a state of tension; but, as Hartsock and McGurl[52] point out, relief of any degree obtained at the expense of drastic curtailment of the subject's activities, defeats its own purposes. Incidentally, Horton[53] has done a real service to histamine desensitization by his illuminating

*The evidence is briefly presented in Appendix IV, and may be read or disregarded, as the reader may wish.

study of the types of headaches which can and cannot be cured by this method.

Butler and Thomas'[20] report on the treatment of migraine by the intravenous administration of histamine includes one particularly striking instance: one of the 34 patients in their series, 63 years old, had had migraine since the age of 15; her mother had committed suicide from this cause, her sister had developed melancholia because of such headaches, and she, herself, had had no relief from morphine. She was completely relieved by histamine therapy.

In the 16 months ending Jan. 1, 1945, I personally treated eight patients with migraine or migraine-like headaches. Six were men and two women, and the age range was from 30 to 54 years. All but two were under 38 years of age. The duration of the headaches ranged from 18 months to 15 years, and the duration of attacks from 24 to 96 hours. Four patients had auras. Two suffered from lacrimation and rhinorrhea, several had impairment of vision during attacks, and one became mentally confused when the pain was at its height. In every instance the attacks had recently been more frequent and more severe. Previous therapy had included various sedatives, morphine, oxygen, ophthalmologic treatment, ergotamine tartrate and, in one instance, submucous resection. In no instance was there any positive physical finding.

All patients were treated by histamine desensitization, for periods ranging from five weeks, in two instances, to 32 weeks in one. There were no reactions. There patients had mild recurrences at the end of two months, three months and four months, respectively; all were promptly relieved by repetition of the desensitization regimen. Four patients have continued maintenance doses of 0.5 cc. for periods varying from 30 to 40 weeks. Results have been good in all cases. The duration of observation ranges from five months in two cases to 12 months in one, and six of the eight patients have been under observation for more than six months.

Migrainous headaches, and headaches produced by the in-

jection of histamine, are to be distinguished from the histaminic cephalgia desribed by Horton,[2] 1939. In both varieties, as von Storch[47] points out, vasodilatation is the cause of the pain, but in Horton's syndrome the pain is sudden, transitory and generalized in all the branches of the internal and external arteries; in migraine, the increase in the amplitude of the cranial arterial pulsations is limited to the branches of the external carotid artery, and the vasodilatation is prolonged, more gradual in onset and likely to be localized.

The syndrome is apparently not frequent. Horton, himself, had observed 72 patients when he made his first comprehensive report, and Baker[54] has reported 30, but Lieder[55] had seen only four cases, and Swanson[56] and Yater[57] only one each. Histamine desensitization was used with generally good results in all the reported cases except Swanson's, in which histaminase produced excellent results after attempted desensitization with histamine had caused a very severe reaction, and in a few of Horton's,[53] in which the same agent was used. It is of interest that Browne,[58] who studied the response to histamine therapy in relation to skin flares in many of Horton's cases, found that every patient who showed an absence of flares or a diminution in their size while under treatment had either complete or partial relief from histaminic cephalgia.

To date I have seen only one case which corresponds with Horton's syndrome (Appendix I). Histamine desensitization gave good results promptly. I have had no personal experience with the syndrome described by Girling[59,60] as "lower half headache." but the reference of symptoms to the sphenopalatine ganglion suggests that this type of headache is a variation of Sluder's[61] syndrome. Histamine desensitization gave complete relief in 15 of 20 cases.

ALLERGIC (VASOMOTOR) RHINITIS.

Aside from the general evidence already listed, there is considerable special evidence for the allergic basis of vasomotor rhinitis. Hansel,[5] who has done much to put the whole sub-

ject on a firm foundation, by a review of microscopic sections from Sluder's[61] material, was able to show that what the latter described as "nonsuppurative infection" manifested by polypoid hyperplasia and neuralgia of the sphenopalatine ganglion, was really allergy, as proved by the preponderantly eosinophilic infiltration in most of the slides. Williams[1] has skillfully established from the clinical standpoint the essentiality of the so-called Sluder syndrome and the syndrome of intrinsic allergy, and Hansel's work, as he points out, puts at least the vasomotor rhinitis component on a firm allergic basis.

The excellent pathologic studies of Finck[62] should be cited in this connection. He was able to show that even in clinically quiescent periods, in which the mucosa of a subject with vasomotor rhinitis is macroscopically normal, microscopic examination shows an increased number of eosinophiles as well as areas of localized edema and increased lymphoid infiltration. Buhrmeister and Wenner[63] identified a histamine-like substance in the nasal mucosa, nasal secretion and nasal polypi, and suggest that alterations in the amount of histamine present in the tissues is probably directly proportional to the degree of injury to the cells. Urbach and Gottlieb[64] have studied the relationship between vasomotor rhinitis and bronchial asthma, the two conditions being associated in more than half of 145 personally studied cases of rhinopathy. Their point that it is much simpler to treat the earlier rhinitis than the later asthma is well taken. Finally, Jackson's[65] observations on anesthetized (usually etherized) dogs showed very great dilatation of the nasal vessels following the injection of histamine.

Characteristically, patients with vasomotor rhinitis, like most other allergic subjects, have usually been treated by many physicians and are none the better but rather worse. Typically, also, the correction of such demonstrable otolaryngologic pathology as may be present does not relieve the symptoms referable to the allergic state. The record of surgical measures is particularly bad, and Hansel[5] and Urbach and Gottlieb,[64] particularly, warn against its promiscuous per-

formance; the latter authors, in fact, do not usually consider it indicated for nasal polypi.

Very favorable results have been reported from histamine desensitization in vasomotor rhinitis by Farmer,[6] Farmer and Kaufman,[37] Williams,[1] Girling,[39,40] and others. Glas, discussing Farmer and Kaufman's[37] contribution in 1942, stated that he had used histamine iontophoresis through the nasal mucosa five years earlier, in desperation and with excellent results. In discussing the same contribution, Cracovaner added his testimony to the excellent results of the method; but Rubenstein,[37] who had used it successfully in Ménière's disease, reported poor results in vasomotor rhinitis, which was attributed by Farmer to his unusually large dosage (200 to 300 gamma). Paterson's[36] results are difficult to evaluate because of the numerous other methods which he employed in all cases.

In the 16-month period ending Dec. 31, 1944, I personally treated 41 patients with allergic rhinitis by desensitization with histamine azoprotein. Twenty-five were men and 16 women. The age range was from 28 to 55 years, and the majority were in the fourth decade. The duration of the disease was difficult to determine in many instances. In two patients it had developed, apparently for the first time, 10 days before and had persisted since. The remainder of the patients had been affected for periods ranging from several months to six years. Nine patients, all of whom had had the condition for several years, had been particularly annoyed by it for several weeks before seeking relief. There was no seasonal incidence.

The history and findings were typical. The usual patient complained of an intermittently "stopped up" nose, sometimes accompanied by sneezing, and of a profuse, watery discharge. If the attack lasted for several days pain was likely to develop over the eyes and through the temples. Many patients were worse at night and were kept awake by the discomfort. Several complained of a postnasal drip, worse at night, and one or two of local itching.

Two patients had had nasal operations, and one had been operated on twice. One patient, with supposed sinus trouble, had moved from Arizona to Louisiana to secure relief. The majority had been treated by various local measures, and many had used various nose drops on their own initiative. A number had been treated by the usual allergic methods, without relief. Three had a family history of allergy.

The nasal mucosa was typically pale, boggy, hyperplastic and edematous; the edema being most marked over the turbinates and frequently causing obstruction of the airways. In two instances polypi were present. The discharge was typically watery, but two patients, who had just had colds of the usual character, had purulent discharges. Except in these two cases, in which neutrophiles predominated, the nasal smears were predominantly eosinophilic.

Allergic testing revealed 12 patients sensitive to dust. In three instances the sensitivity was associated with food sensitivities; in two, with sensitivity to smoke; in two, with sensitivity to bacteria, and in one, with sensitivity to pollen. One patient was sensitive to a fungus for which no vaccine was available. The other patients in this group were treated by obvious allergic methods, without notable improvement. The same was true of the five cases in which autogenous vaccines were used. Bilateral antral puncture in one case did not relieve symptoms, nor did the use of special nose drops in six cases.

All the patients, after the measures described had failed, were desensitized with histamine azoprotein, according to the regimen described. The duration of treatment ranged from one week in one patient to 20 weeks in two. Thirty-three were treated for periods ranging from 11 to 13 weeks.

All patients were eventually relieved, though two had recurrences, at six weeks and three months, respectively; the former had discontinued treatment against advice. Three patients took maintenance doses of 0.5 cc. weekly for periods ranging from 12 weeks to 36 weeks after the completion of the usual courses. The period of observation ranges from

four to 20 months and six months or more in all but nine cases. Twelve patients have been followed for a year or more.

Special cases are presented in Appendix I.

AURAL DERMATITIS.

Good results in various allergic skin lesions have been reported with the histamine desensitization method by Alexander and Elliott,[34] Sheldon and his associates,[27] Smith,[67] Girling[40] and Jenkins.[68] I have personally used the method in 12 instances of dermatitis localized in and about the ear. With one exception, a patient who treated herself with drops secured on advice of a druggist, all the patients had been under competent medical supervision before I saw them, but autogenous vaccines, chemotherapy (sulfonamides and penicillin), light therapy and local measures of various kinds had been ineffective. Four patients were men and eight women, and the age range was from 18 to 42 years. The duration of the skin lesions varied from four weeks to 20 years.

Physical examination was negative in all cases except for the local condition. The auditory canal was always excoriated and frequently contained débris. The tympanic membrane, which in several instances was perforated centrally, was reddened and edematous. The meatus was fissured in several cases and in several the whole auricle was desquamated.

In view of the failure of other methods, desensitization with histamine azoprotein was employed without delay in almost every case, the injections usually being given twice daily unless a reaction required less rapid medication. No other measures were employed except local cleansing. The duration of treatment extended from one week in one case to 12 weeks in one case, nine patients were treated between five and seven weeks. Results were prompt in every case, improvement frequently being noted as early as the fourth injection. There has been no recurrence in any case during the period of observation, which has ranged from three months in two cases to 16 months in one case; six patients have been under observation six months or longer.

Illustrative cases are appended (Appendix I).

SUMMARY AND CONCLUSIONS.

1. Evidence for the allergic basis of certain conditions which frequently come to the attention of the otolaryngologist is briefly outlined. These conditions, which in some instances occur in combination, are vertigo, which may or may not take the form of Ménière's disease; periodic headaches, which may or may not take the form of migraine; and vasomotor (allergic) rhinitis.

2. Evidence is presented to indicate that the explosive release of histamine from the tissue cells is the basis of the allergic reaction.

3. The rationale of desensitization by histamine in allergic states is presented. It is emphasized that this method is particularly useful in instances of multiple sensitivity, and in the rather frequent instances in which the causative allergens cannot be demonstrated.

4. The writer's personal experience with desensitization by histamine azoprotein is presented. Over the 16-month period ending January 1, 1945, he has treated, with generally good to excellent results, 40 cases of vertigo, nine cases of periodic headaches, including one case of histaminic cephalgia, and 41 cases of vasomotor rhinitis. A brief statement is also made concerning 12 cases of aural dermatitis treated by the same method. Approximately 40 cases treated since the stated date, with equally satisfactory results, were not included in the discussion because of the brevity of the period of observation.

5. Reactions which occurred in the series are tabulated in detail. None was serious and only a few required control by epinephrine.

6. The writer's favorable experience with this method, which is substantiated by the experience of others (briefly outlined), suggests a more extended trial of desensitization by histamine particularly in the form of histamine azoprotein, in so-called "intrinsic" allergy.

APPENDIX I – ILLUSTRATIVE CASE REPORTS* – VERTIGO.

Case 1: A white boy, 13 years of age, had had severe vertigo and nausea for 24 hours, regardless of position; he could not sit, stand or move unless firmly upheld. Treatment by sedatives had been ineffective. The only finding on examination was a third degree nystagmus, with the quick component to the left, and impaired hearing, of which he had not complained. Audiometric testing showed a 30 db loss (straight across) in the left ear for all frequencies, and a 15 db. loss in the right ear. The intravenous administration in hospital of histamine diphosphate (1 cc. in 250 cc. of physiologic salt solution, 10 drops to the minute) relieved the vertigo almost immediately. Desensitization with histamine azoprotein was then undertaken by the regimen described. Audiometric testing two months after the initial attack revealed no impairment of hearing, and there has been no recurrence of vertigo and no impairment of hearing in the ensuing 22 months.

Case 2: A white man, 43 years of age, had been under ophthalmologic study for positional vertigo, which had been present for six months and was associated with a sense of fullness and impairment of hearing on the left side. Examination revealed a left maxillary sinusitis and congestion of the left Eustachian tube. Neither vertigo nor deafness was relieved by left antral puncture, with demonstrable clearing of the sinus, or by inflation of the tube. The patient was then desensitized with histamine azoprotein by the regimen described and had complete relief of both symptoms for 13 months. At the end of this period vertigo recurred in a milder form, and audiometric examination again showed a loss of higher frequencies on the left. Desensitization was repeated (in dosages stepped up from 0.05 to 0.5 cc.), again with complete relief of both vertigo and audiometric impairment The patient has been kept on a maintenance dose of 0.5 cc. of histamine azoprotein weekly and has had no recurrence of symptoms in the ensuing eight months.

Case 9: A white woman, 53 years of age, had been confined to bed for 10 days with nausea and vertigo of such a degree that she could not move her head. Sedation and other remedies by her family physician had produced no relief whatsoever, but she had complete relief after the sixth subcutaneous injection (0.5 cc.) of histamine azoprotein. She discontinued treatment against advice after the eleventh dose, as she regarded herself as cured. A mild recurrence of the original symptoms seven weeks later was checked by a second course of injections, concluding with a weekly maintenance injection of 0.5 cc. for 12 weeks. She has remained well for a year.

Case 10: A white woman, 38 years of age, for three weeks had had positional vertigo, with the feeling that she was going to faint. Several members of her family had histories of allergy. Desensitization with histamine azoprotein was begun. Following a severe local reaction after the eleventh dose there was a prompt improvement of all symptoms. The patient discontinued treatment after the sixth week of maintenance therapy, regarding herself as cured, and has remained symptom-free for 19 months.

Case 13: A white woman, 34 years of age, had had vertigo, nausea, fullness in the left side of the head, and pain in and around the left eye, for six weeks. The vertigo was constant, but the pain was most severe between 10 A.M. and 2 P.M. Treatment with various nose drops had

*Only essential positive data are stated.

been completely ineffective. Examination revealed a pale, boggy nasal mucosa, with polypoid formation, and washing of the left maxillary sinus produced about four drams of foul, milky pus. Chiefly because of the appearance of the nasal mucosa and the polypoid formation, desensitization with histamine azoprotein was instituted. After the ninth injection all symptoms disappeared and the nasal mucosa became a healthy pink. Although the sinus condition has persisted, the patient has been completely relieved of vertigo and pain for 14 months.

Case 22: A white male, 34 years of age, for three weeks had had vertigo, greatly aggravated by the slightest change of position. He was under traetment for "allergic colitis" and had a childhood history of asthma. The nasal mucosa was pale and hyperplastic. Desensitization with histamine azoprotein was begun by the usual regimen. On the fifth injection (0.4 cc.) he had a severe reaction, with increased vertigo, nausea, headache and flushing. He refused treatment for the next week. Therapy was then resumed with 0.3 cc. of histamine azoprotein, and six injections were given at this level without reaction, followed by a weekly maintenance dose at the same level for the next eight weeks. The patient has been completely relieved of all symptoms, including those due to "colitis," for nine months.

Case 24: A white woman, 28 years of age, had had vertigo, greatly aggravated by any change of position, and a sense of fullness in both ears for four weeks. Treatment by nicotinic acid had been ineffective. The nasal mucosa was pale and hyperplastic, and both Eustachian tubes were occluded. Inflation of the tubes precipitated a very severe attack of vertigo, which was followed by transient relief of this symptom. Desensitization with histamine azoprotein produced some relief of the recurrent vertigo, though progress was less prompt and less spectacular than usual. In the meantime, the allergic examination had revealed sensitivity to the cosmetics being used. When they were changed, continuation of desensitization completely relieved the vertigo, and the patient has remained well for 13 months except for transient fullness in the ears after contact with the offending cosmetics.

PERIODIC HEADACHE.

Case 3: A white woman, 34 years of age, had had periodic headaches at least once a month for the past 18 months. Recently they had been more frequent and more severe. The pain, which was chiefly on the left side, extended into the eye, and at the height of the attack vision was impaired and she was greatly confused mentally. Attacks were preceded by malaise and a sense of extreme uneasiness and were associated with nausea and vomiting. Ergotamine tartrate and oxygen therapy had given occasional relief during the attacks, but the results were not impressive. Allergic study revealed sensitivity to dust and a few foods, but treatment along these lines was ineffective. Desensitization with histamine azoprotein was then carried out over a period of nine weeks. For the past seven months the patient has had no headaches at all, though on three occasions, when she experienced premonitory symptoms, a prophylactic injection of 0.5 cc. of histamine azoprotein was given.

HISTAMINIC CEPHALGIA.

Case 1: A nun, aged 30 years, had had frequent unilateral headaches for the past 18 months. They appeared abruptly and were associated with blockage of the nasal canal, profuse rhinorrhea and lacrimation on the affected side. Usually the attacks lasted only a few hours, but on

two or three occasions had lasted 36 hours. Desensitization with histamine azoprotein checked the attacks on the seventh injection (0.06 cc.) and there has been no recurrence for 11 months.

ALLERGIC RHINITIS.

Case 4: A white male, 36 years of age, had had a "stuffy nose" as long as he could remember. It had been persistent for the last six weeks. At intervals there were episodes of sneezing and rhinorrhea. The nasal mucosa was pale and hyperplastic and smears were predominantly eosinophilic. Allergic study was positive for dusts and a few foods, but therapy by the accepted methods produced no results. Desensitization with histamine azoprotein was carried out over a period of 13 weeks, and the patient has been symptom-free for 16 months.

Case 5: A white woman, 34 years of age, had had a stopped-up nose with pains through the eyes and temples at intervals "for more years than she could remember." Her symptoms had been much worse in the last few weeks. The nasal mucosa was pale and hyperplastic and smears were predominantly eosinophilic. Allergic examination was positive for dust and smoke but a fair test of therapy along these lines produced no results. Desensitization with histamine azoprotein was carried out by the usual regimen and the patient has remained symptom-free for 15 months.

Case 6: A white woman, 29 years of age, had had a stopped-up nose and attacks of sneezing and rhinorrhea for six years, much worse in the last three months, and so much worse at night that she had to discontinue her usual occupation (private duty nursing). The nasal mucosa was pale and boggy, and there was a profuse watery discharge. Allergic study was positive for dust and a few pollens. A test of allergic therapy (which had previously been ineffective) produced no results, but improvement was almost immediate when desensitization with histamine azoprotein was undertaken. A severe local reaction occurred on the eighth injection (0.7 cc.). The patient requires treatment with pollen extract when certain pollens are in season, and at these times is given occasional maintenance doses of histamine azoprotein, but otherwise she has been completely symptom-free for 18 months.

Case 9: A white woman, 52 years of age, had had a "snuffy" nose and recurrent attacks of sneezing and rhinorrhea for six years. Her family history was positive for allergy, and she had been treated by allergic methods, but without results. The nasal mucosa was pale, the meati were filled with polyps, and there was clinical evidence of secondary infection. The nasal smears showed neutrophiles as well as eosinophiles Roentgenologic examination revealed a pansinusitis.

Since allergic testing showed sensitivity to dust and bacteria, therapy along these lines was instituted but produced no results. Desensitization with histamine azoprotein was then begun. The patient had asthmatic attacks, readily relieved by adrenalin, with injections of 0.2 cc., 0.4 cc., and 0.7 cc. Because the dosage had to be stepped up cautiously for this reason, treatment covered a period of 20 weeks. The patient, however, declared that the reactions did not trouble her at all because she felt better than she had felt at any time in the last six years. Following the cessation of treatment she continued to have occasional mild blockages of the nasal canal, of no comparable severity to those previously experienced, and occasional mild asthmatic attacks. When penicillin became available she was treated with it, because her sinus condition had not

cleared up under other forms of therapy, and since that time she has been perfectly well. The period of observation in this case covered 20 months.

Case 13: A white woman, 34 years of age, presented the usual symptoms of allergic rhinitis, which had been present "for years." Both nasal canals were completely obstructed by boggy, edematous mucosa, with no evidence of secondary infection. Desensitization with histamine azoprotein was undertaken by the usual routine and the patient was completely relieved for three months. Her symptoms recurred after the emotional disturbances accompanying a death in the family, and desensitization was repeated. The first injection (0.5 cc.) precipitated an asthmatic attack, readily controlled with adrenalin. Injections were resumed in the amount of 0.05 cc., and the dosage was cautiously increased to 0.5 cc. The patient has been symptom-free for seven months.

AURAL DERMATITIS.

Case 1: A white woman, 39 years of age, had had a dermatitis involving the left auricle for three weeks. It had become rapidly worse in spite of treatment with sulfathiazole and other local measures. Examination revealed excoriation of the left auditory canal; injection and thickening, without perforation, of the tympanum; several fissures at the meatus; and desquamation of the entire auricle. All therapy was discontinued except for local cleansing measures but at the end of a week the condition had continued to progress. Desensitization with histamine azoprotein was then begun, by the usual regimen except that injections were given twice daily. Improvement was evident on the sixth injection. There has been no recurrence of the condition over a 19-month period of observation.

Case 4: A white woman, 28 years of age, following a right mastoidectomy at the age of eight, had had intermittent drainage from the skin and an almost continuous dermatitis on this side. Recent treatment with boric acid and alcohol had greatly aggravated it. The right auditory canal was swollen and excoriated and excoriations were present on the bowl of the auricle. The tympanum was centrally perforated and the middle ear was wet. Routine therapy for the middle ear condition promptly cleared it up, but the dermatitis was unaltered by any form of treatment. At the end of 10 days all other therapy was discontinued and desensitization with histamine azoprotein was carried out, as in Case 1. Results were apparent on the sixth injection, and there has been no recurrence of the lesion, which had existed for 20 years, in the eight months since treatment was discontinued.

APPENDIX II.

Although it is difficult to ascribe to any single individual the credit for the first description of the anaphylatic and allergic reactions, experimental and clinical observations[7-12] carried out over the last four decades have justified the assumption, to quote Zinsser's statement of the postulate, that allergy in man "is based on an immunological mechanism basically identified with anaphylaxis in animals, superficially modified by human anatomical and physiological conditions."

Dale and Ladlaw,[8] in 1910, noted "as a point of interest and possible significance" the fact that the immediate symptoms with which an animal responds to the injection of a normally inert protein to which it has been sensitized are "to a large extent" those of poisoning by beta in imazolyl-ethylamine, that is, histamine. It was not until 1929, however,

that Dale,[9] "on a platform of plausibility and congruity," as Dragstedt[10] well expresses it, formulated the theory of anaphylaxis as the result of cell injury due to the intracellular reaction of an antigen with an aggregating antibody. In the meantime, Lewis and Grant[11] had concluded that the specific response of local anaphylaxis in the human skin represents a special form of cell injury leading to the release of "H-substance," to which this name was given because its pharmacologic behavior was indistinguishable from that of histamine.

A considerable body of evidence[7,10] now exists that this substance actually is histamine. Initial attempts to identify it in the circulating blood during anaphylactic shock and allergic reactions did not succeed, because, as Dragstedt[10] has pointed out, it was not realized how brief was its presence under the circumstances. When this fact was comprehended, and when adequate testing methods were devised,[7] it was found uniformly whenever an appreciable reaction had occurred, the increase in blood histamine varying according to the species tested. While Rose's application to human subjects of the Code test for histamine has produced results which are not accepted uniformly, they do prove, as Code grants, that in certain allergic conditions the histamine mechanism of the body is definitely disturbed. From these and other studies, Code continues, two conclusions are warranted: *1.* That histamine is released during acute allergic reactions as a consequence of damage to cells already containing histamine. *2.* That the release of histamine from the cells under these circumstances is rapid and explosive and, as experimenta evidence proves, may be in sufficient quantity to kill the animal. What permanent cellular damage is residual in surviving animals is still to be demonstrated.

APPENDIX III — HISTAMINE AZOPROTEIN.

Fell and his associates[23,24] reasoned that a rational approach to the problem of an effective histamine preparation would be to combine histamine with a protein, to form an antigenic complex which would engender antibodies whose specificity would be determined by the histamine (hapten) portion of the molecule. Theoretically, immunization with such a complex would develop antibodies of the desired specificity. Such antibodies should neutralize any excess histamine released after an antigen-antibody reaction and thus would prevent the symptoms of anaphylactic or allergic reactions, even though the genesis of the reaction, so to speak, had occurred. This idea was based on the discoveries of Landstein in 1936 concerning the immunologic specificity of artificial antigens.

The first preparation, a compound of histamine with casein, a protein which is seldom responsible for human allergic reactions, was satisfactory experimentally but discouraging clinically. Horse serum, from which the serum specificity had been largely eliminated by the "despeciation process, was then used instead of casein. Two conjugates were prepared: a complex product formed by coupling an isocyanate derivative of histamine with despeciated globulin and a second compound, histamine azoprotein, produced by coupling histamine to despeciated serum by means of the diazo reaction.

Tests on the guinea pig ileum in the Schultz-Dale apparatus showed that histamine azoprotein[23] contains practically no free histamine; it contains from 0.8 to 1 mg. of bound histamine (as the free base) per cubic centimeter. Guinea pigs which had been rendered histamine refractory by histamine azoprotein were later sensitized (actively and pas-

sively) with ovalbumin, then were injected intravenously with shocking doses of the same substance. Most of the control animals died of anaphylactic shock. The histamine-resistant animals not only survived but presented only mild anaphylactic reactions, if any at all.

A series of observations by Cohen and Friedman[25,26] also demonstrated the efficacy of histamine azoprotein. Precipitins in the serum of allergic subjects desensitized by this method proved at least partially specific for histamine, while *in vitro* and *in vivo* studies indicated that histamine neutralization can occur after desensitization with histamine azoprotein.

Sheldon and his associates[27] made the first clinical tests with hapamine on 39 subjects with atopic eczema, physical allergy, seasonal hay fever, perennial allergic rhinitis, migrainous headache and contact dermatitis. Without other treatment except for local measures in atopic eczema and contact dermatitis, they obtained most encouraging results, particularly in the latter disease.

APPENDIX IV – THE ALLERGIC BASIS OF PERIODIC HEADACHE.

The extensive experimental and clinical studies of Wolf and his co-workers[40-45] have done much to elucidate the etiology of migraine and other periodic headaches and to explain the basis of the pain. Headache not due to organic causes, such as brain tumor or aneurysm, is primarily caused by vasodilatation. Such an etiology explains the clinical observation, made by many victims for themselves, that pressure on certain superficial cranial vessels greatly relieves their symptoms. The distribution of the pain depends upon the special artery affected. Clark and his associates[40] were able to show the intimate relationship between the severity of the special attack and the amplitude of the artery, which in turn indicated the degree of vasodilatation. They were also able to duplicate attacks by mechanical distention of the superficial temporal artery.

Torda and Wolff[45] have pointed out that after several hours of a severe headache, the cranial vessels appear prominent and distended, and are rigid, pipe-like and difficult to compress, in contrast to their normally compressible state. The frequent observation that after several hours of pulsating, throbbing pain the headache often takes the form of steady pain these authors explain as the result of thickening and edema of the muscular and adventitial vascular structures. They proved their postulate by the examination of sections taken from temporal arteries during migrainous attacks, and point out that this demonstration makes clear why ergotamine tartrate, which is generally used for the relief of migrainous headache, is effective only when it is given early in the attack.

The allergic basis of headache was first proposed by Lesne and Richet, Jr. (cited by Thomas and Johnston[49]), in 1913. Vaughan,[46] who was the first to treat headaches by allergic methods, found in a study made in 1935 that at least 7 per cent of a rural community of 508 persons had suffered at one time or another from recurrent headaches due to specific food idiosyncrasies, and stated that headaches of this kind are considerably more frequent in allergic subjects than in the population at large.

The precipitating cause of the vasodilatation believed to be responsible for migrainous headaches is the release of histamine into the blood

as the result of an allergic reaction. The evidence for this theory has been excellently reviewed by Williams,[1] among others, but one or two particularly significant observations should be mentioned.

Von Storch,[47] in a series of ingenious studies, found that the threshold for histamine-produced headache is lower in persons subject to chronic, recurrent headaches than in those not so afflicted, and even lower in those subject to true migraine than in those not subject to it. In patients subject to migraine the type of headache produced by histamine was frequently similar to their usual headaches, but histamine-produced hearache was only occasionally similar to their usual hearaches in those who suffered from the nonperiodic variety.

Goltman's[48] case, although a single instance, is a remarkable demonstration of the mechanism of migrainous headache. A 26-year-old woman, with a personal and family history of allergy, had suffered from migraine since childhood. She was operated on in the course of a severe headache, on the suspicion of brain tumor. The operative findings included a tight and nonpulsating dura; greatly dilated vessels; the escape of a quantity of clear fluid under pressure when the dura was opened and when the left ventricle was punctured; and a "wet" brain. In the five years following the operation the course of events before, during and after an attack of migraine was always the same: The depression in the left frontal region at the site of the incision began to fill up as the headache came on, assumed the aspect of a visible and palpable, tense, fluctuating tumor during the attack, and resumed its original appearance as the attack receded. The patient, who was found to be allergic to 26 substances, was completely relieved by allergic therapy and the phenomena described ceased to appear.

Several points made by Atkinson[32] in the course of the presentation of his dual theory of etiology of migraine and Ménière's disease are pertinent. He believes the two conditions are related because: *1.* The affected regions are not far apart from the standpoint of vascular supply, both being supplied by branches of the basilar artery, and the chief pathologic difference between the two diseases is in the point of impact, which is the occipital lobe in migraine and the labyrinth in Ménière's disease. *2.* The age incidence of both diseases helps to prove the relationship, migraine being a disease of earlier and Ménière's a disease of later life. *3.* One condition often merges into the other, or both may exist spontaneously, as age advances. *4.* The cyclic vomiting of childhood may be an initial phase of the same allergic process.

REFERENCES.

1. Williams, Henry L.: Intrinsic Allergy as It Affects the Ear, Nose and Throat: The Intrinsic Allergy Syndrome. *Ann. Otol., Rhinol. and Laryngol.*, 53:397, 1944.

2. Horton, Bayard T.: The Use of Histamine in the Treatment of Specific Types of Headaches. *Jour. A. M. A.*, 116:377, 1941.

3. Piness, George, and Miller, Hyman: Allergy of the Upper Respiratory Tract in Infancy and Childhood. *Jour. A. M. A.*, 113:734, 1939.

4. Richards, Lyman: Four Decades of Nasal Allergy. *Arch. Otolaryngol.*, 39:465, 1944.

5. Hansel, F. K.: Allergy of the Nose and Paranasal Sinuses: A Monograph on the Subject of Allergy as Related to Otolaryngology, St. Louis, The C. V. Mosby Co., 1936.

6. FARMER, LAURENCE: Histamine in Anaphylaxis and Allergy. *Bull. N. Y. Acad. Med.*, 16:618, 1940.

7. CODE, CHARLES F.: The Mechanism of Anaphylactic and Allergic Reactions. An Evaluation of the Rôle of Histamine in Their Production. *Ann. Allergy*, 2:457, 1944.

8. DALE, H. H., and LAIDLAW, P. P.: The Physiological Action of *B*-imina-zolylethylamine. *Jour. Physiol.*, 41:318, 1910.

9. DALE, H. H.: Croonian Lectures on Some Chemical Factors in the Control of the Circulation. *Lancet*, 1:1179, 1233, 1285, 1929.

10. DRAGSTEDT, CARL A.: The Significance of Histamine in Anaphylaxis. *Jour. Allergy*, 16:69, 1945.

11. LEWIS, THOMAS, and GRANT, R. T.: Vascular Reactions of the Skin to Injury. VII. Notes on the Anaphylactic Skin Reaction. *Heart*, 13:219, 1926.

12. KATZ, GERHARD: Histamine Release from Blood Cells in Anaphylaxis *in Vitro*. *Sci.*, 91:221, 1940.

13. KATZ, GERHARD, and COHEN, STANLEY: Experimental Evidence for Histamine Release in Allergy. *Jour. A. M. A.*, 117:1782, 1941.

14. KATZ, GERHARD: Histamine Release in the Allergic Skin Reaction. *Proc. Soc. Exper. Biol. and Med.*, 49:272, 1942.

15. BEST, C. H., and MCHENRY, E. W.: Histamine. *Physiol. Rev.*, 11:371, 1931.

16. RAMIREZ, M., and ST. GEORGE, A. V.: A Contribution to the Etiology of Asthma. *Med. Jour. and Rec.*, 119:71, 1924.

17. HORTON, T. B., and BROWN, G. E.: Systemic Histamine-like Reactions in Allergy Due to Cold. Report of Six Cases. *Am. Jour. Med. Sci.*, 178:191, 1929.

18. DEUTSCH: Cited by Williams.[1]

19. BEST, C. H., *et al.*: The Nature of Vasodilator Constituents of Certain Tissue Extracts. *Jour. Physiol.*, 62:397, 1929.

20. ROTH, G. M., and HORTON, B. T.: Physiologic Effects of Histaminase and Histamine. *Jour. A. M. A.*, 114:522, 1940.

21. ALEXANDER, H. L.: Treatment of Allergic Disorders with Histamine and Histaminase. *Jour. Lab. and Clin. Med.*, 26:110, 1940.

22. PESHKIN, M. M.; RAPAPORT, H. G.; MESSER, WILLIAM; FEUER, IRVING; SICULAR, ADELE, and BERGER, ARTHUR: Histaminase in the Treatment of Allergy in Children. *Jour. Pediat.*, 22:426, 1943.

23. FELL, NORBERT; RODNEY, GERTRUDE, and MARSHALL, DONALD E.: Histamine-Protein Complexes: Synthesis and Immunologic Investigation. I. Histamine-Azoprotein. *Jour. Immunol.*, 47:237, 1943.

24. RODNEY, GERTRUDE, and FELL, NORBERT: Histamine-Protein Complexes: Synthesis and Immunologic Investigation. II. *B*-(5-Imidazolyl) Ethyl Carbamido Protein. *Jour. Immunol.*, 47:251, 1943.

25. COHEN, MILTON B.: The Immunologic Management of a Patient wieh Allergy. *Jour. Allergy*, 15:274, 1944.

26. COHEN, MILTON B., and FRIEDMAN, HAROLD J.: Immunity Against H-Substance. *Jour. Allergy*, 15:245-248, 1944.

27. SHELDON, J. M.; FELL, N.; JOHNSTON, J. H., and HOWES, H. A.: A Clinical Study of Histamine Azoprotein in Allergic Disease. *Jour. Allergy*, 13:18, 1941.

28. Furstenberg, A. C.; Lashmet, F. H., and Lathrop, Frank: Ménière's Symptom Complex; Medical Treatment. *Ann. Otol., Rhinol. and Laryngol.*, 43:1035, 1934.

29. Shea, John J.: The Office Treatment of Vertigo (Histamine Therapy). The Laryngoscope, 52:362, 1942.

30. Butler, Stuyvesant, and Thomas, William A.: Intravenous Histamine in the Treatment of Migraine. *Jour. A. M. A.*, 128:173, 1945.

31. Horton, B. Y., *et al.*: A Symposium on Ménière's Symptom Complex. *Arch. Otolaryngol.*, 40:329, 1944.

32. Atkinson, Miles: Ménière's Syndrome, Migraine and Certain Related Conditions. *Jour. Med. Soc. N. J.*, 41:11, 1944.

33. Horton, Bayard T.: The Use of Histamine in Ménière's Disease. *Surg., Gynec. and Obst.*, 72:417, 1941.

34. Alexander, H. L., and Elliott, R. W.: Treatment of Chronic Urticaria with Intravenous Injections of Histamine. *Jour. A. M. A.*, 114:522, 1940.

35. Rainey, John J.: Histamine in the Treatment of Ménière's Syndrome. *Jour. A. M. A.*, 122:850, 1943.

36. Shea, John J.: The Therapy of Histamine and Nicotinic Acid. The Laryngoscope, 55:325, 1945.

37. Rubenstein, H. J., in discussion of Farmer, Laurence, and Kaufman, Robert E.: Histamine in the Treatment of Nasal Allergy (Perennial and Seasonal Allergic Rhinitis). The Laryngoscope, 52:255, 1942.

38. Ingham, Donald W.: Ménière's Syndrome. Report of Two Cases Treated with Histamine Administered Intravenously. *Med. Assn., Dist. of Columbia*, 9:241, 1940.

39. Turvey, S. E. C.: Ménière's Syndrome with the Results of Treatment with Histamine. *N.W. Med.*, 43:203, 1944.

40. Clark, Dean; Hough, Heloise, and Wolff, H. G.: Experimental Studies on Headache. Observations on Headache Produced by Histamine. *Arch. Neurol. and Psychiat.*, 35:1054, 1936.

41. Ray, Bronson S., and Wolff, Harold G.: Experimental Studies on Headache. Pain-Sensitive Structures of the Head and Their Significance in Headache. *Arch. Surg.*, 41:813, 1940.

42. Schumacher, G. A.; Ray, B. S., and Wolff, H. G.: Experimental Studies on Headache. Further Analysis of Histamine Headache and Its Pain Pathways. *Arch. Neurol. and Psychiat.*, 44:701, 1940.

43. Schumacher, George A., and Wolff, Harold G.: Experimental Studies on Headache. A. Contrast of Histamine Headache with the Headache of Migraine and That Associated with Hypertension. B. Contrast of Vascular Mechanisms in Preheadache and in Headache Phenomena of Migraine. *Arch. Neurol. and Psychiat.*, 45:199, 1941.

44. Wolff, Harold G.: Headache — Mechanisms and Differential Diagnosis. *Clin.*, 2:1394, 1944.

45. Torda, C., and Wolff, H. G.: Experimental Studies on Headache: Transient Thickening of Walls of Cranial Arteries in Relation to Certain Phenomena of Migraine Headache and Action of Ergotamine Tartrate on Thickened Vessels. *Arch. Neurol. and Psychiat.*, 53:329, 1945.

46. Vaughan, Warren T.: An Analysis of the Allergic Factor in Recurrent Paroxysmal Headaches. *Jour. Allergy*, 6:365, 1935.

47. von Storch, Theodore J. C.: Relation of Experimental Histamine Headache to Migraine and Nonmigraine Headache. *Arch. Neurol. and Psychiat.*, 44:316, 1940.

48. Goltman, Alfred M.: The Mechanism of Migraine. *Jour. Allergy*, 7:351, 1936.

49. Thomas, J. W., and Johnston, C. R. K.: Headaches of Allergic Origin. *Med. Clin. N. Amer.*, 24:285, 1940.

50. Derbes, Vincent J.; Engelhardt, Hugo T., and Watters, Theodore A.: The Management of Migraines. *South. Med. Jour.*, 38:533, 1945.

51. Patzer, Reynold, and Engelhardt, Hugo: Periarterial Infiltration in the Diagnosis and Treatment of Migraine: Experimental and Clinical Experiences with Eucupine and Procaine Hydrochloride. *Arch. Surg.*, 50:296, 1945.

52. Hartsock, C. L., and McGurl, F. J.: Allergy as a Factor in Headache. *Med. Clin. N. Amer.*, 22:325, 1938.

53 Horton, Bayard T.: Symposium: Head and Face Pain. Medicine. *Trans. Amer. Acad. Ophthalmol.*, p. 1, 1944.

54. Becker, B. M.: The Treatment of Periodic Headaches by Injections of Histamine. *Trans. A. Amer. Phys.*, 55:294, 1940.

55. Lieder, Louis E.: Histaminic Cephalalgia and Migraine. *Ann. Int. Med.*, 20:752, 1944.

56. Swanson, L. W.: Histaminic Cephalalgia. *Jour. Allergy*, 15:144, 1944.

57. Yater, W. M.: The "Vascular" Headache. Report of a Case Successfully Treated with Histamine. *Med. Assn. Dist. of Columbia*, 9:165, 1940.

58. Browne, Harry C.: Cutaneous Reactions as an Index to Desensitization to Histamine. *Jour. Allergy*, 14:19, 1942.

59. Girling, Moray: Lower Half Headache. *N.W. Med.*, 41:418, 1942.

60. Girling, W. N. M.: Administration of Histamine in Allergic Conditions. *N.W. Med.*, 42:196, 1943.

61. Sluder, Greenfield: The Rôle of the Sphenopalatine (or Meckel's) Ganglion in Nasal Headaches. *N. Y. Med. Jour.*, 87:989, 1908.

62. Finck, Harry P.: Tissue Changes in the Nasal Mucosa. *Trans. Amer. Laryngol., Rhinol. and Otol. Soc., Inc.*, p. 63, 1927.

63. Buhrmeister, Catherine C., and Wenner, W. F.: Presence of a Histamin-like Substance in Nasal Mucosa, Nasal Polypi and Nasal Secretion. *Arch. Otolaryngol.*, 24:570, 1936.

64. Urbach, Erich, and Gottlier, Philip M.: The Relation of Vasomotor Rhinitis to Bronchial Asthma. *Arch. Pediat.*, 59:382, 1942.

65. Jackson, D. E.: Experimental and Clinical Observations Regarding the Physiology and Pharmacology of the Nose. *Ann. Otol., Rhinol. and Laryngol.*, 51:973, 1942.

66. Paterson, W. P. E.: Vasomotor Rhinitis. *Canad. Med. Assn. Jour.*, 52:400, 1945.

67. Smith, L. M.: Histamine in the Treatment of Atopic Dermatoses. *Arch. Dermat. and Syph.*, 44:883, 1941.

68. Jenkins, Edward C.: Preliminary Report on the Treatment of Postarsenical Dermatitis with Histamine. *Ven. Dis. Inform.*, 24:11, 1943.

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THE NASOPHARYNX.
A STUDY OF 140 AUTOPSY SPECIMENS.*

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Our knowledge of the nasopharynx is meager as compared to that of other organs. Neither the rhinologist nor the pathologist has taken advantage of available material, autopsy and clinical, for careful investigation and study. While the clinician has been taught to examine the nasopharynx in the course of routine diagnosis, he frequently neglects this structure in searching for the cause of many general medical problems. The pathologist, on the other hand, has deliberately passed over this organ, partially because of its relative inaccessibility but more especially because a satisfactory technique for its removal had not been devised.

My primary objective is to record the pathologic findings in 140 autopsy specimens of the nasopharynx. These findings have borne out the belief that the nasopharynx is a more important structure than has hitherto been appreciated. This is particularly significant from the standpoint of its pathologic processes, as has been appropriately emphasized by Kline.[1] It is, moreover, an important structure clinically. There are a number of pathologic processes which involve the nasopharynx and usually go unrecognized. Hill analyzed the causes of the diagnostic pitfalls and mentioned four: not looking, not seeing, not knowing what to look for, and not interpreting correctly what is seen. If the situation is such that neglect and failure are the main reasons for our restricted familiarity with the nasopharynx, it behooves us to increase our knowledge of this organ. This is essential not only to improve our treatment of the local processes but also to remove from the sphere of obscurity the relationship of these processes to other body diseases.

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Obviously, not every phase of the nasopharynx and its diseases can be considered in a limited paper. I shall, therefore, restrict myself to a brief discussion of the fundamental aspects and of the major pathologic processes encountered in the present autopsy study.

PERTINENT APPLIED ANATOMY.

The nasopharynx is defined by Callender[2] as a cube-shaped organ, the direct posterior continuation of the nasal fossa.

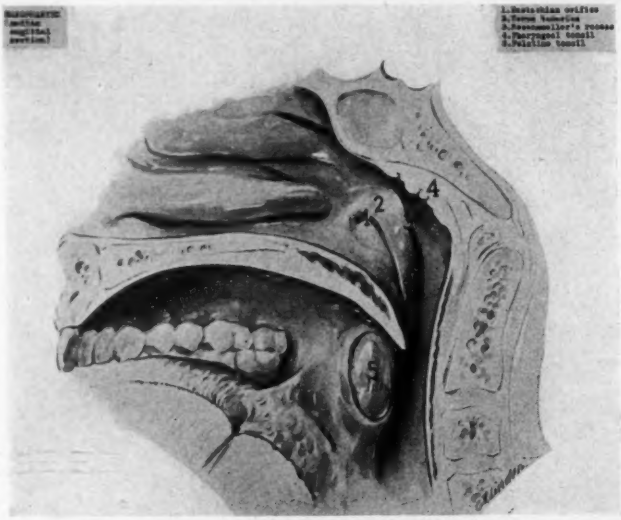

Fig. 1. The nasopharynx — medial sagittal section.

Morris[3] states that the nasal pharynx (pars nasalis) belongs with the nasal fossa as a part of the respiratory rather than the digestive system. It is described by most authors as a musculomembranous tube placed behind the nasal cavities, mouth and larynx (see Figs. 1 and 2).

The separations between the three divisions of the pharynx are purely arbitrary. During the act of swallowing, the nasopharynx is separated from the oropharynx by the soft palate and uvula which are pressed against the contracting muscular posterior wall.

According to Schiller,[4] the shape and size of the nasopharyngeal cavity is determined largely through the configuration of the surrounding bony structures. The *roof* of the cavity is formed by the lower surface of the body of the sphenoid bone, the *posterior wall* by the basilar part of the occipital bone, the anterior arch of the atlas and the body of the second cervical vertebra. The arch may be palpated a little below the roof of this space. The protrusion of this anterior arch may be the responsible factor in stenosis of the nasopharyngeal space.

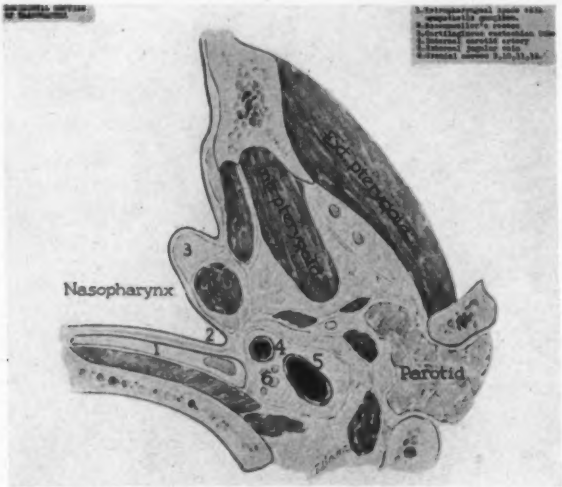

Fig. 2. Horizontal section of nasopharynx — relation to adjacent anatomic structures.

Testut[5] describes three forms of the pharyngeal arch, *viz.*, the angular, the rounded and the low. With the angular arch the roof of the pharynx slants backward and downward and forms a very blunt angle with the posterior wall. With the rounded arch the roof of the pharynx rises to a medium height above the level of the palate. The low arch, characteristic of infancy, is situated at the level of the inferior turbinate with the tubal opening at the level of the palate. This latter type, however, may disappear in adults. The signifi-

cance of the small, shortened nasopharynx, the so-called infantile nasopharynx, was stressed by Bernfeld.[6] He remarked that *complete* adenoidectomy is often difficult in a narrow nasopharyngeal cavity.

The walls of the nasopharynx consist of a strong fibrous membrane which Testut,[5] as well as other authors, calls "pharyngeal aponeurosis." Cunningham[7] describes the upper part of the pharyngeal aponeurosis as strong to maintain the integrity of the wall of the pharynx where the muscular fibres

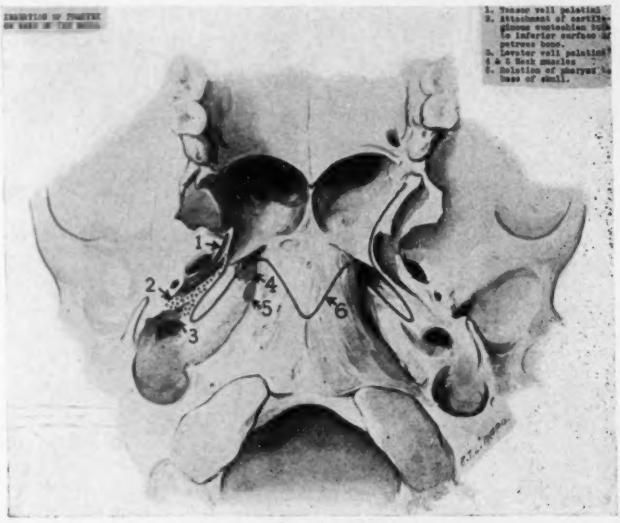

Fig. 3. Insertion of pharynx on base of skull.

of the superior constrictor are absent. "As it passes downward, it gradully becomes weaker, until it is ultimately lost as a distinct layer. It lies between the muscles and the mucous membrane and is visible from the outside of the pharynx, only where the muscles are absent. It is the principal means by which the pharynx is attached to the base of the skull (see Fig. 3), and it is united also to the auditory tubes and the bony margins of the choanae."

The pharyngeal aponeurosis is considered by Testut[5] as the tendon of insertion for the constrictor muscles of the pharynx, which are covered externally by a thin fascial layer. At its superior part it passes forward on the surface of the buccinator muscle and is termed the "buccopharyngeal fascia." The pharyngeal aponeurosis and the buccopharyngeal fascia blend into one layer near the base of the skull where the superior constrictor muscle is deficient on each side. The term "sinus of Morgagni" is applied by Cunningham to the semi-

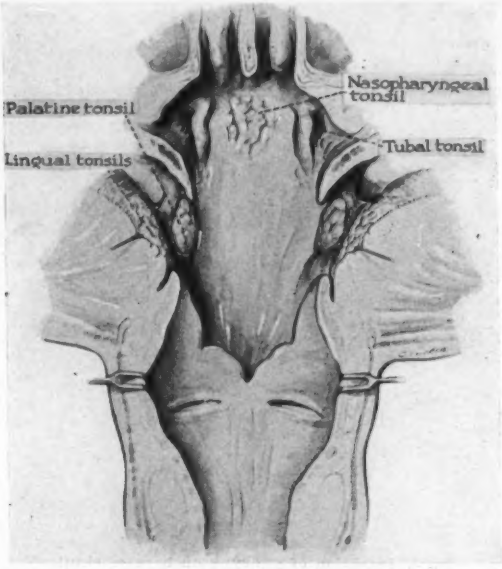

Fig. 4. Lymphatic ring of Waldeyer; the pharyngeal tonsil and the other lymphatic structures.

lunar interval which intervenes between the base of the cranium and the upper crescentic margin of the superior constrictor. He states that the deficiency in the muscular wall of the pharynx in that region is compensated for by the increased strength of the pharyngeal aponeurosis, which in that situation is called the pharyngobasilar fascia.

The lateral walls of the nasopharynx present certain struc-

tures of practical importance to the otolaryngologist. On each wall is situated the opening to the auditory (Eustachian) tube and the tubal elevation (torus tubarius). Posterior to these structures is a slit-like space, the fossa (recess) of Rosenmüller. Inflation of the auditory tubes assumes a knowledge of their exact situation and relationship to adjacent and neighboring structures. While in infancy and childhood the openings of the auditory tubes are at a level of the palate, in adult life the situation of these openings attains the level of the posterior ends of the inferior turbinates. Obstruction of these auditory openings by hypertrophy or infection of the surrounding lymphatic tissue leads to impairment of hearing. The tubes form the route by which an infectious process in the nasopharynx travels to the middle ear.

The posterior wall of the nasopharynx presents a prominent lymphoid structure, especially in childhood, the pharyngeal tonsil (see Fig. 4). When this lymphoid mass becomes abnormally enlarged, it produces *adenoids*. It is usually atrophied in adults, but in numerous instances hypertrophy instead of atrophy has been found, even in the seventh decade of life. Adenoids may be so extensive as to fill out the entire nasopharynx and encroach on its walls. Above the pharyngeal tonsil a flack-like depression may extend to the basilar process of the occipital bone. This structure is known as the *pharyngeal* or *nasopharyngeal bursa*.

HISTOLOGIC ESSENTIALS.

The mucosa of the nasopharynx consists of an epithelial layer and a lamina propria. The muscular coat is absent, being sustituted by a well developed elastic layer forming a sharp demarcation between the mucosa and the submucosa, and in areas in which the submucosa is absent between the mucosa and the muscular layer. The submucosa is present only in the lateral walls of the nasopharynx, especially in the walls of Rosenmüller's fossa (recess). The muscular layer consists of striated muscle arranged in two layers — an internal with longitudinal fibres (stylopharyngeus and palatopharyngeus) and an external layer formed by the superior

pharyngeal constrictor muscle. The external layer of the nasopharynx is the tunica adventitia. Since the superior constrictor muscle does not reach the base of the skull, the upper part of the posterior wall of the nasopharynx is formed by the pharyngobasilar fascia. This structure consists of the lamina propria (mucosa) in the form of a thick elastic layer, and of the tunica adventitia.

Inasmuch as the muscular coat is deficient at this level, the lamina propria and the adventitia are directly adjacent to each other, and this constitutes the roof of the nasopharynx in the mid-dorsal area (fornix). By this structural arrangement the nasopharynx is virtually suspended to the undersurface of the base of the skull.

In the nasopharynx three types of epithelium may be differentiated. The transition between them shows differences which are distinctly individual. In the vault of the nasopharynx is found the typical respiratory type of epithelium (pseudostratified ciliated) with numerous goblet cells. On the lateral walls the ciliated epithelium extends to the ostia of the Eustachian tubes and even further caudad. The remainder of the nasopharyngeal cavity is lined by stratified squamous epithelium. The narrow strip of transition between these two different types of epithelium is formed by stratified columnar epithelium. The fossa of the pharyngeal tonsil is lined with ciliated epithelium; however, lateral to the pharyngeal tonsil the lining consists of stratified squamous epithelium.

The glands are of the mucous and mixed varieties. The latter are typical for the respiratory tract. The pure mucous glands lie below the elastic layer; the mixed glands above this layer. While the mixed glands are especially prominent and well developed below the pharyngeal tonsil, the mucous glands are in a similar state in the submucosa of Rosenmüller's fossa (recess) and in the plica salpingopharyngea.

Lymphocytic infiltration of the mucosa is characteristic for various areas of the nasopharynx, especially in the region of the pharyngeal ostium of the Eustachian tube. The torus tubarius, for example, may be provided with lymph nodules

which in their totality are correctly considered as "tubal tonsil."

PATHOLOGIC CONSIDERATIONS AND PATHOLOGIC FINDINGS.

The nasopharynx is frequently the seat of inflammation or tumors, while injuries play a minor rôle. An inflammatory process may originate in the nasopharynx itself or extend into it from adjacent structures. The inflammation may be acute or chronic. Acute inflammation of the nasopharynx usually is a part of an acute inflammatory process of the entire pharyngeal mucosa, or of Waldeyer's ring. Chronic inflammation of the nasopharynx is either specific or nonspecific.

TABLE 1. PATHOLOGIC FINDINGS IN 140 AUTOPSY SPECIMENS OF THE NASOPHARYNX.

Tuberculosis of the nasopharynx	18
Hyperplasia of the nasopharyngeal tonsil	9
Hyperplasia of tubal tonsil	4
Pharyngeal bursa —	
Small	6
Large	4
Marked adhesions in recess of Rosenmüller	7
Cysts of the nasopharynx —	
In area of nasopharyngeal tonsil	2
In recess of Rosenmüller	1
Follicular pharyngitis	3
Cyanotic induration of nasopharyngeal mucous membrane	3
Hyperkeratosis of nasopharyngeal mucous membrane	1
Metastatic carcinoma	1

Thus it will be seen that of 140 specimens, 59, or approximately 48.5 per cent, showed evidence of some form of pathology. It is interesting to note, furthermore, that the more prominent pathologic processes were tuberculosis, pharyngeal bursitis and hyperplasia of the nasopharyngeal tonsil.

Among the specific inflammations, syphilis, rhinoscleroma and lymphogranuloma are of importance. Chronic inflammation of the nonspecific type is attributable to a chronic irritation of the mucosa, which, in turn, is due to an infectious secretion originating in a neighboring cavity, and draining into the nasopharynx. The source of this secretion may be the posterior ethmoid or sphenoid sinuses, the nasal chambers, or the tympanic cavities.

Of the benign tumors, hypertrophy of the nasopharyngeal tonsil is of most frequent occurrence. For this reason if for

no other, it is, therefore, of considerable interest and importance. Next to the adenoids, cysts, choanal polyps and fibromas merit attention. The incidence of malignant tumors is greater than generally believed. Of these, carcinoma and lymphosarcoma must receive first consideration.

Table 1 summarizes the gross pathologic findings in 140 consecutive autopsy specimens from adult patients who expired from various diseases in hospitals for mental disorders. Most of the subjects were past middle life, some in the seventh and eighth decades.

Since these conditions are to be discussed separately, comment will be reserved for these discussions.

It should be stated here that the nasopharynx was removed by a new technique[8] whereby the organ itself and its important adjacent structures are completely preserved. This is definitely essential for complete study.

TUBERCULOSIS OF THE NASOPHARYNX.

Tuberculosis of the nasopharynx (see Fig. 5) is only meagerly described in textbooks on pathology and otolaryngology. While routine autopsy examinations of the nasopharynx have been performed by few investigators, histologic examination of the adenoids removed surgically has been done by several workers.[9,10] Dietrich,[11] in 1916, briefly discussed tuberculosis of the nasopharynx and differentiated tuberculosis of the mucous membrane from tuberculosis of the nasopharyngeal tonsil. Trenis,[12] in 1940, reported two cases of tuberculosis of the nasopharynx with positive sputum findings and negative Roentgen examination of the chest.

My interest in nasopharyngeal tuberculosis was aroused in the course of a routine pathologic study of autopsy specimens of the nasopharynx. There were 24 cases of pulmonary tuberculosis found in the total number of (140) specimens, 18 of which showed definite evidence of tuberculous disease in the nasopharyngeal cavity. The pathologic process was generally an ulcerative lesion on the posterior part of the roof and of

the upper part of the posterior wall. Less frequently, tuberculous lesions were found on the posterior margin of the ostia of the Eustachian tubes and the nasopharyngeal surface of the uvula and soft palate.[13]

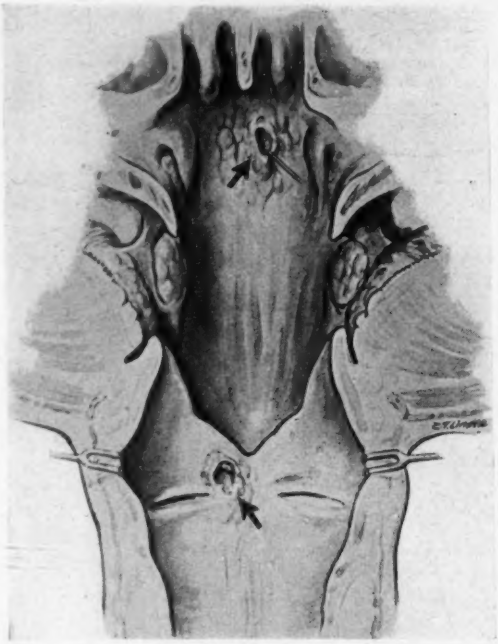

Fig. 5. Tuberculosis of the nasopharynx — ulcerative type of lesion.

The importance of histopathologic study is shown through the circumstance that in four of our cases only careful microscopic examinations of the material from several blocks revealed tuberculous changes (see Table 2). In this connection the studies of Gräff[14] are of interest, since they gave similar results. In 118 subjects with open active tuberculosis of the lungs, he noted gross lesions in 36 per cent, while by histopathologic study tuberculous findings were confirmed in a total of 82 per cent.

TABLE 2. VARIATION IN INCIDENCE OF TUBERCULOSIS OF THE NASOPHARYNX ON THE BASIS OF GROSS AND HISTOLOGIC CHANGES.

Type of Pulmonary Tuberculosis	Gross Changes	Histologic Changes	Other Extra-Pulmonary Involvements
Far advanced fibrocaseous ulcerous	18	13	Yes
Fibrotic	2		Yes
Fibrotic, with beginning of fibrocaseous changes	1	1	
Fibrotic with exudative pleuritis	1		
Miliary	1		

The nature of the gross pathologic changes is of paramount importance for the clinical recognition of the disease. Such gross changes are characterized by irregular ulcers, ordinarily ovoid, with undermined margins and yellowish-gray bases. Histopathologic changes embrace the following: Subepithelial tubercles composed of epitheloid cells, giant cells, incipient or advanced caseation necrosis. It should be mentioned, however, that the histologic changes were observed primarily in the remnants of the lymphatic tissue (see Fig. 6).

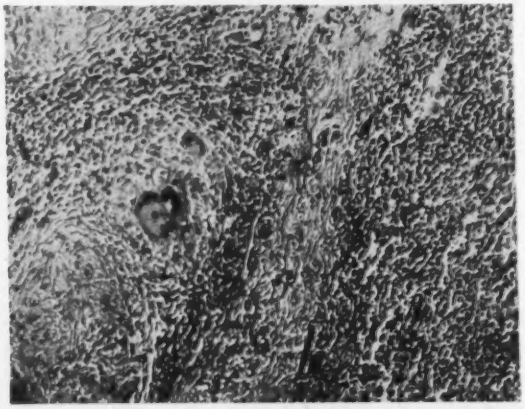

Fig. 6. Histopathologic section of posterior part of roof of nasopharynx from 65-year-old male with fibrotic type of pulmonary tuberculosis.

Oropharyngeal tuberculosis has been more commonly recognized than the nasopharyngeal type. There were, however, no cases in our autopsy material. Because of the difficulty in

visualization of the nasopharynx, lesions in this area are commonly overlooked. When ulcerations in the nasopharynx occur, they are usually an indication of severe general disease.[15] The nasopharynx is commonly the source of positive sputum. In all cases of pulmonary tuberculosis, routine examination must include complete investigation of the nasopharyngeal cavity.

From the present study it would seem that tuberculosis of the nasopharynx occurs more frequently than tuberculosis of the larynx. At least this has been the finding in our pathologic investigations. Whether this finding corresponds with the results of clinical examinations only further studies will reveal. Two types of nasopharyngeal tuberculosis should be differentiated, *viz.*, the *open* or ulcerous, and the *closed*, which is discernible only by microscopic examination.

LYMPHOID HYPERPLASIA.

As far as lymphoid hyperplasia of the nasopharynx is concerned, the autopsy specimens presented a number of variations from the common teachings. First of all, the frequent incidence of hyperplasia of the nasopharyngeal or the tubal

TABLE 3.[20] DISTRIBUTION OF THE STAGES OF DEVELOPMENT AND INVOLUTION OF LYMPHATIC TISSUE (WALDEYER'S RING) IN 140 AUTOPSY SPECIMENS ACCORDING TO AGE GROUPS.

	20-35	35-50	50-65	65-75	Over 75
Nasopharyngeal tonsil —					
Completely involuted	5	10	37	32	16
Partially involuted	2	4	8	9	5
Moderately well developed	....	....	2	1	....
Well developed, hyperplastic	3	1	1	1	3
Tubal tonsil —					
Involuted	9	14	44	40	17
Partially involuted	....	2	3	....	3
Moderately developed	1	....	1	1	1
Well developed, hyperplastic	1	2	....	....	1
Palatine tonsil —					
Involuted or very small	1	1	5	5	4
Small or moderately developed	6	12	39	35	14
Hyperplastic	3	2	5	2	6
Lingual tonsil					
Moderately developed	8	15	39	38	18
Well developed, hyperplastic	3	1	9	5	4

tonsils, or both, in adults should be pointed out. It should be stated that while the literature[16,17,18] contains occasional ref-

erence to hypertrophy of the nasopharyngeal tonsil in older persons, even after the sixth or seventh decade of life, only in a very few instances have the statements advanced been substantiated by specific studies.

From present observations one must concur with the views of Mathias that hyperplasia of the nasopharyngeal tonsil may

Fig. 7. Specimen from a woman 75 years of age; **A**, Nasopharyngeal tonsil showing marked hyperplasia; **B**, septum nasi; **C**, posterior wall of the pharynx; **D**, epiglottis.

occur independently, or may be a part of a general hyperplasia of Waldeyer's ring (see Fig. 4).

Table 3[20] details the incidence of partial and of complete hyperplasia of the lymphoid structure of Waldeyer's ring according to different age groups. It is of special interest to

note the incidence of hyperplasia of the nasopharyngeal tonsil in persons past 70 years of age (see Fig. 7).

Histologic examination of numerous sections revealed large numbers of follicles with germinative centers. The follicles were separated from one another. The lymphoid tissue of the mucosa was covered by ciliated columnar epithelium. In some instances small cyst-like structures were present. The cysts were lined with columnar epithelium. From this description it may be assumed that the morphologic picture of nasopharyngeal lymphoid hyperplasia of adults is practically the same as that of adenoid vegetations of childhood.

Hyperplasia of the tubal tonsil was found less frequently than hyperplasia of the nasopharyngeal tonsil. In the specimens examined for this study there were only four specimens of the tubal tonsil presenting hyperplasia, compared with nine specimens of the nasopharyngeal tonsil. Partial involution of the nasopharyngeal tonsil was a common observation. Experience has demonstrated that hyperplasia of the nasopharyngeal tonsil is not always associated with clinical symptoms. Infections may, however, influence their production. Pressure symptoms may result from crowding of the contents of the nasopharyngeal vault. Hyperplasia of the tubal tonsils is significant because of its relation to the ostiums of the Eustachian tubes. This has been recognized as a common cause of obstructive deafness in children but has been given insufficient consideration as an etiologic factor of deafness in older persons.

Bojkay[21] thinks it is unusual to find adenoid vegetations in persons over 30 years of age. He cites two cases of hypertrophy of the pharyngeal tonsil; one a woman, age 51, and one a man, age 33 years. The symptoms complained of were obstruction to nasal breathing, dull voice, impaired hearing, otalgia and nervous disorders.

PHARYNGEAL BURSITIS (THORNWALDT'S DISEASE).

According to Huber,[22] the pharyngeal bursa arises at a point on the posterior wall of the nasopharynx (see Fig. 8), where the pharyngeal segment of the notochord has retained

its connection with the pharyngeal ectoderm. Thornwaldt,[23] in 1885, reported his findings in 25 patients with disease of the so-called nasopharyngeal bursa. von Luschka[24] described the bursa as an elongated pocket lined with epithelium and

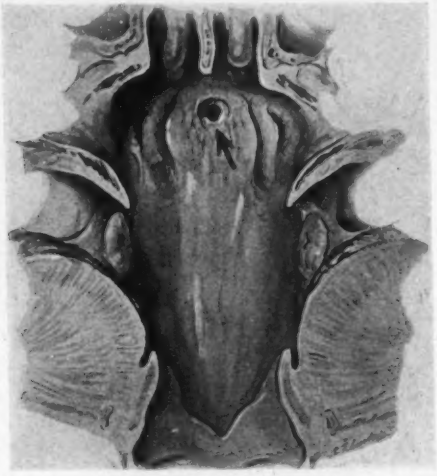

Fig. 8. Pharyngeal bursa.

with an orifice situated in the midline at the lower border of the pharyngeal tonsil, extending backward and attached to the periosteum of the occipital bone. According to Dorrance,[25] the term "bursa pharyngea" designates a sac-like depression in the posterior wall of the nasopharynx just above the uppermost fibres of the superior constrictor muscle, and usually extending upward and backward toward the occipital bone, which it sometimes reaches with its apex (see Fig. 9).

It should be stressed that a nasopharyngeal bursa is in itself not pathologic. Eagle[26] states in this connection: "Apparently the sac does not become infected or cause any symptoms as long as there has been no trauma, such as must occur in the scraping of adenoid tissue." In the greater portion of Eagle's cases, clinical symptoms and the presence of a bursa were noted mainly in those patients in whom adenoids had been

removed. Only when inflammation, infection or cyst formation occurs in the bursa is the condition recognized as so-called Thornwaldt's disease.

Of the 10 bursae found in the 140 specimens on which this present study is based, there were six small ones, 3 mm. or less in diameter, and four large ones (*i.e.*, larger than 3 mm. in diameter). An inflammatory or infectious process in the

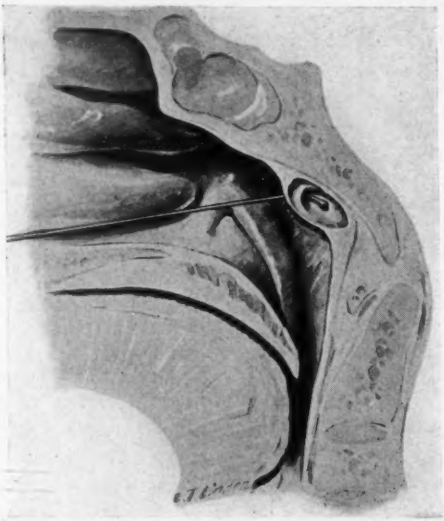

Fig. 9. Pharyngeal bursa showing sac-like depression in the posterior wall of nasopharynx, with insertion of probe.

median recess may give the same major symptoms as a pharyngeal bursitis; in fact, this was found to be true in two of the specimens. For this reason it is essential either to differentiate the two conditions histologically, or to consider them strictly from a clinical point of view and substitute for Thornwaldt's disease the term "Thornwaldt's syndrome," more accurately to describe the process.[27]

The main symptoms, occipital headache and postnasal drip, are suggestive of the nasopharyngeal affection. Godwin[28]

observed in five of seven patients a characteristic headache syndrome in the pharyngeal bursa group. The characteristic symptoms noted were: *a.* Persisting dull-aching or throbbing occipital headache localizing below the external occipital protuberance; *b.* stiffness or soreness of the posterior cervical muscles; *c.* exacerbations of pain on movement of the head.

The histopathologic observations are of interest. When remnants of the nasopharyngeal tonsil are detected, one must conclude that the specimen is not from a pharyngeal bursa but from a median recess; *i.e.*, a result of involution of the nasopharyngeal tonsil. Grossly, specimens from either a bursa or a median recess resemble each other. They are diverticular-like structures situated in the midline of the nasopharynx between its superior and posterior walls. Usually the diverticulum is filled with mucous plugs and there are adhesions to Rosenmüller's fossa (recess).

Yankauer[29] expressed the opinion that a nasopharyngeal abscess develops from the median recess, while Kully,[30] Dorrance[25] and Eagle believe that the pathologic changes arise from the nasopharyngeal bursa.

Finally, it may be said from the investigations of Dorrance,[25] and from the observations and studies of other workers that the bursa is not the same structure referred to as Seessel's pocket and Rathke's pouch, nor is it a true median recess. It is acknowledged, however, that a similarity of symptoms and of gross pathologic characteristics exists irrespective of the site of the infectious process; *i.e.*, the median recess or the bursa.

CYSTS.

Cysts of the nasopharynx are relatively uncommon and frequently overlooked, according to Kully.[30] They may arise from any of the nasopharyngeal structures, including the bursa. In the autopsy material of the present study there were found two cases of nasopharyngeal cysts in the area of the nasopharyngeal tonsil (see Fig. 10), and one case in Rosenmüller's fossa.

Cysts of the nasopharynx may be grouped in five categories:

1. Those with smooth surface, originating in the bursa.

2. Those surrounded by adenoids—so-called retention cysts (two were found in autopsy specimens).

3. Small cysts due to retention in the mucous glands—

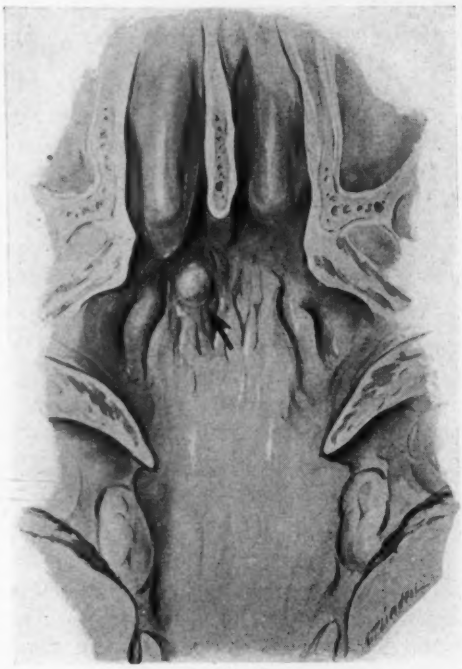

Fig. 10. Cyst of nasopharynx.

so-called true retention cysts, being obliterations of the ducts of the mucous glands (one found in autopsy specimens).

4. Degenerative cysts in which there is a necrosis of the adenoid tissue itself, and the cyst cavity is lined with adenoid tissue.

5. Branchiogenic cysts — usually rare — in the region of the Eustachian cushions.

Nasopharyngeal cysts may result from various causes. The cysts may contain pathogenic organisms, more especially hemolytic streptococci. In one of our cases these organisms were found on culture. Nasopharyngeal cysts may be the source of a generalized infection; for example, rheumatic fever.

The more important type of cysts of the nasopharynx is the retention cyst in the residual adenoid. It has been described by Yankauer. Cysts in the nasopharynx may be due to the persistence of a bursa. This type of cyst is from 1 to 2 cm. in diameter and has a small opening in its center. It contains thick, gelatinous material and often streptococci. These cysts may be the source of a postnasal discharge, affect the middle ear, or act as a focus of infection generally.

MALIGNANT NEOPLASMS.

It is well known that both benign and malignant tumors are found in the nasopharynx. Since our study was performed on consecutive autopsies without reference to any nasopharyngeal disease during life, obviously no large number of cases with neoplasms was to be anticipated.

There was only one case of carcinoma of the nasopharynx (see Fig. 11), and mention is made of it merely to point out the remoteness of metastatic involvement, the primary focus being in the rectum.

This case, therefore, emphasizes again the importance of complete examination of the nasopharynx in every instance where metastatic involvement of a malignant new growth is suspected.

The vast majority of malignant tumors of the nasopharynx are epithelial in origin and fall into the group of squamous-celled carcinoma. In a series of 50 cases of malignant neoplasms of the nasopharynx studied by Hauser and Brownell,[31] carcinoma was the diagnosis in 46, three were called lymphoblastoma, and one was diagnosed myeloma.

These authors stress the significance of cervical enlargement and involvement of the cranial nerves at the base of the brain — a full-fledged syndrome of nasopharyngeal malignancy,[32] as they put it — rendering the diagnosis rather simply. The diagnosis becomes increasingly difficult, however, if no irritation of the nerves or loss of function is present. Tit-

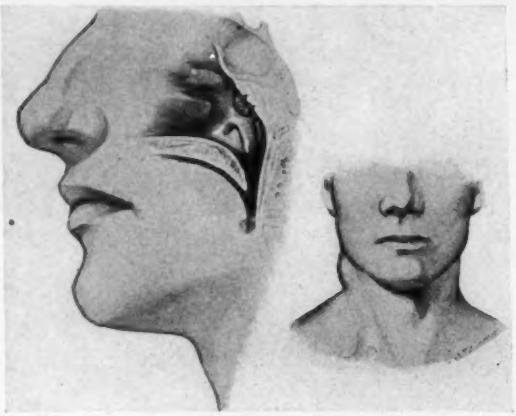

Fig. 11. Carcinoma of nasopharynx.

rud and Peyton[33] also describe the neurologic complications of nasopharyngeal tumors, but imply that such complications are not always present. In their series of 195 cases, neurologic symptoms were present in 63 per cent of the cases of squamous cell carcinoma, and in 73 per cent of the cases of lymphoepithelioma.

SUMMARY.

1. The primary objective of this paper is to record the pathologic findings in 140 autopsy specimens of the nasopharynx.

2. The anatomy, histology and pathology are discussed, and the pathologic findings in 140 autopsies tabulated.

3. There were 24 cases of pulmonary tuberculosis found in the total number of specimens and 18 of these gave definite

gross or microscopic evidence, or both, of tuberculosis of the nasopharynx.

4. As far as lymphoid hyperplasia of the nasopharynx is concerned, this study revealed the frequent incidence of hyperplasia of the nasopharyngeal or the tubal tonsils, or both, in older persons, even in the sixth or seventh decades of life.

5. While 10 pharyngeal bursae were found in the 140 specimens, histologic examination of several specimens revealed the fact that the characteristic symptoms of pharyngeal bursitis may be simulated by an inflammatory or infectious process in the median recess.

6. Cysts of the nasopharynx may arise from any of the nasopharyngeal structures, including the bursa, and may be due to various causes.

7. The present study revealed only one case of carcinoma of the nasopharynx, mention of which is made merely to point out the remoteness of metastatic involvement, the primary focus being in the rectum.

Due acknowledgment is made to Dr. Paul B. Szanto for his aid in accumulating the material and for collaboration in the pathologic study.

REFERENCES.

1. KLINE, O. R.: Importance of Pathologic Conditions of the Nasopharynx to the Otolaryngologist. *Arch. Otolaryngol.*, 41:140, Feb., 1945.

2. CALLANDER, C. L.: Surgical Anatomy. W. B. Saunders, Philadelphia, 1939.

3. MORRIS, SIR HENRY: Human Anatomy. P. Blakiston, Son and Co., 1933.

4. SCHULLER, A.: Weber die Rontgen untersuchung des Epipharynx. *I Cong. internat. otorhinolaryngol.*, 286, 1929.

5. TESTUT, LEO: Traité d' anatomie humaine. G. Doin æ Cie., Paris, 1928-1931.

6. BERNFELD, K.: Klinische Studies zur Frage des infantillen Nasopharynx. *Monatsschr. f. Ohrenh.*, 611, 1926.

7. Cunningham's Practical Anatomy. William Wood and Co., New York, 1926.

8. SZANTO, P. B.: A Modified Technique for the Removal of the Nasopharynx and Accompanying Organs of the Throat. *Arch. Pathol.*, 38:313, Nov., 1944.

9. WHITE, E. M.: Pathology of Adenoids and Adenoid Tuberculosis. *Am. Jour. Med. Sci.*, 134:228, 1907.

10. LACHMAN, J.: Untersuchungem ueber die latente Tuberculose der Rachenmandeln Inaug.-Dis. Leipzig.

11. DIETRICH, A.: Der Pharynx. *Hdb. d. spez. path. Anat. Hist.*, 4:12. J. Springer, Berlin, 1936.

12. TRENIS, W. J.: Tuberculosis of the Nasopharynx, Positive Sputum with a Roentgenographically Negative Chest. *Am. Jour. Med. Sci.*, 199:312, Mar., 1940.

13. SZANTO, P. B., and HOLLENDER, A. R.: Tuberculosis of the Nasopharynx. *Ann. Otol., Rhinol. and Laryngol.*, 53:508, Sept., 1944. HOLLENDER, A. R., and SZANTO, P. B.: Tuberculosis of the Nasopharynx. Its Frequent Incidence and Clinical Significance. *Dis. Chest*, 11:227, May-June, 1945.

14. GRAFF, S.: Die Bedeutung des Epipharynx fur die Pathologie. *Klin. Wchnschr.*, 15:953, July 4, 1936.

15. MYERSON, M. C.: Tuberculosis of the Ear, Nose and Throat. J. C. Thomas, Springfield, 1944.

16. HOFMAN, C. M.: Die Adenoiden Tumoren als Teilerscheinung der Hyperplasie des lymphatischen Rachenringes und in ihren Beziehungen zum ubrigen Korper, Halle, a, S., K. Marhold, 1895; Samml. Zwangl, Abhandl. a. d., *Geb. d Nasen-, Ohren-, Mund- u. Halskr.*, 1:5-6, 1895.

17. EPHRAIM, E.: Casuistische Mittheilungen. *Monatsschr. f. Ohrenh.*, 33:198, 1899.

18. FRANK, P.: Hypertrophische Rachenmandeln bei Greisen. *Arch. f. Laryngol.*, 18:285, 1906.

19. MATHIAS, W.: Ueber den Entwicklungsgang des Waldeyerschen Rachenringes. *Beitr. z. path. Anat. u. z. allg. Path.*, 94:389, 1935.

20. HOLLENDER, A. R., and SZANTO, P. B.: Lymphoid Hyperplasia of the Nasopharynx. *Arch. Otolaryngol.*, 41:291, Apr., 1945.

21. BOJKAY, T.: Adenoid Vegetations in Elderly Persons. *Arch. Ohrenh. u. Heilk.*, 145:92, July, 1938.

22. HUBER, G. C.: On the Relation of the Chorda Dorsalis to the Analge of the Pharyngeal Bursa or Median Pharyngeal Recess. *Anat. Rec.*, 6:373, 1912.

23. THORNWALDT, G. L.: Ueber die Bedeutung der Bursa pharyngea fur die Erkennung und Behandlung gewusser Nasenrachenraumkrankheiten. J. F. Bergmann, Wiesbaden, 1885.

24. VON LUSCHKA, H.: Der Schlundkopf des Menschen. Laupp, Tubingen, 1868.

25. DORRANCE, G. M.: The So-called Bursa Pharyngea in Man. *Arch. Otolaryngol.*, 13:187, Feb., 1931.

26. EAGLE, W. W.: Pharyngeal Bursae (Thornwaldt's Bursae); Report of 64 Cases. THE LARYNGOSCOPE, 49:199, Mar., 1939.

27. HOLLENDER, A. R., and SZANTO, P. B.: Thornwaldt's Syndrome. *Ann. Otol., Rhinol. and Laryngol.*, 54:575, Sept., 1945.

28. GODWIN, R. W.: Thornwaldt's Disease. Characteristic Headache and Etiology. THE LARYNGOSCOPE, 54:66, Feb., 1944.

29. YANKAUER, S.: Nasopharyngeal Abscesses. A Report of 155 Cases. *Trans. Am. Acad. Ophth. and Otolaryngol.*, 34:364, 1929; *Ann. Otol., Rhinol. and Laryngol.*, 39:481, June, 1930.

30. KULLY, B. M.: Cysts and Retention Abscesses of the Nasopharynx. *Jour. Otol. and Laryngol.*, 50:317, 1935.

31. HAUSER, I. J., and BROWNELL, D.: Malignant Neoplasms of the Nasopharynx. *Jour. A. M. A.*, 27:2467, Dec., 1938.

32. NEW, G. B.: Syndrome of Malignant Tumors of the Nasopharynx *Jour. A. M. A.*, 79:10, July, 1922.

33. TITRUD, L. A., and PEYTON, W. T.: Nasopharyngeal Tumors and Their Neurologic Complications. *Jour. Nerv. and Ment. Dis.*, 92:727, Dec., 1940.

605 Lincoln Road.

J. BISHOP ANNOUNCES FIRST HYPONEEDLE WITH PLASTIC HUB.

The first postwar improvement in hypodermic needles, a needle with the first plastic hub, was announced by Paul C. Kerk, president of J. Bishop and Co., Platinum Works. The hub of the Albalon needle, as the company calls this innovation, is made of gleaming white plastic nylon. The needle itself is of stainless steel and is so beveled as to cleanly pierce and spread the epidermis without undue cutting, slicing or bruising the skin. This also provides a less painful injection.

The plastic hub withstands all commonly used methods of sterilizing, eliminates freezing of hub and syringe tip and thus tends to reduce breakage of syringe from this cause. Leakage around syringe tip is also minimized by the elastic qualities of the Albalon hub. The company has just released the Albalon needle for distribution through the usual trade channels, and will promote the sales of this and the Bishop production in the leading medical and hospital journals.

WHAT THE OTOLOGIST SHOULD KNOW ABOUT THE EDUCATIONAL PROBLEMS OF DEAFNESS.*

HARRIET MONTAGUE,
Los Angeles, Calif.

For many years I have held successive positions that had to do with the effect of deafness on the individual. These jobs began where the physician had left off. They dealt with young mothers to whom otologists had said, "Your child is deaf; there is no possible cure," or with adults to whom a doctor had delivered a shattering ultimatum: "You have a form of deafness for which no cure has been found. Your hearing loss may remain stationary, or it may increase; but it is very unlikely that you will grow better."

I admire very much the courage of a physician who will tell his patient the truth and not hold out false hopes; but I have wished hundreds of times that he had not stopped with that bald statement, "There is no cure." If only he had gone on to tell his patients what life still held for them, and had assured them that deafness, even profound deafness, is not an insurmountable calamity! If only he had proceeded to build a bridge, right there in his office, from the medical to the educational side of deafness; from despair, in fact, to hope and promise — how much it would have meant to his patient! There is scarcely a deaf or hard-of-hearing person in the world for whom something may not be done educationally; and if the otologist were fully informed as to the vehicles by which his patient might proceed to the educational end of the bridge, how much he might facilitate that passage! There are a few outstanding physicians who try to show their patients constructive possibilities ahead of them, but not many go out of their way to do this, and it is to them that these suggestions are offered.

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*Excerpts from this paper were delivered at a Symposium on Hearing conducted at the University of Southern California, Los Angeles, Calif., March 12, 1946.

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Take the young mother who has just been told that her two- or three-year-old boy or girl — or, as frequently happens now, her one-year-old baby — is deaf. The mother's first thought, of course, is medical treatment — a cure — and if one doctor tells her he cannot cure her child, she goes to another, and another. I know one mother who took her two-year-old boy to 12 otologists in succession. All of them told her the same thing — that her child would always be deaf — but not one told her that there were great possibilities in education for the deaf; not one mentioned the fact that there was a great deal she, herself, could do for the boy and that the sooner she began the better it would be, both for her and the child. All these doctors were in or near New York City but not one of them directed the mother to the many schools for the deaf in that area.

How easy it would have been for one of them to say: "Talk to him. Keep right on talking to him, even though he is deaf! He will learn to read many words from your lips, and you will be surprised at the amount you can get across to him, if you will just talk to him. Make sure he is looking at you, and that the light is on your face; also, be sure he knows what you are talking about. If you say 'Ball,' show him a ball. If you say 'Shoe,' point to his shoe. But don't ever stop talking to him!" I have never heard of any doctor saying that to any mother. On the contrary, I know of a physician who said to a mother, whose little boy already had the beginnings of a lip-reading vocabulary, "Why do you keep talking to him? He is stone deaf."

Even the otologists who mention schools are too apt to say, authoritatively, "When he is six, you can send him to the state school for the deaf. Until then, there is nothing you can do." One mother that I know protested against this dictum and insisted that she wanted to do something right away. The otologist replied, "There isn't a school for the deaf in the country that will take him before he is six years old." This was in Denver, where there is an oral day school that accepts children of three; and it was just a year ago, when there were already many schools throughout the United States with

nursery school departments open to children even as young as two-and-a-half.

Only the other day, I saw a letter written by an Army major, an otologist, who had examined the three-year-old child of an Army private here in California. The letter read, in part: "In my opinion, this child will never hear nor speak. When he is six years old, he will be eligible to attend the state school for the deaf and dumb. There are day schools, but they prefer hard-of-hearing children who have some speech."

These statements are misleading, to put it mildly. There is no longer a school in the United States that may properly be referred to as a "school for the deaf and dumb," because every school for the deaf has taken legal measures to remove the word "dumb" from its title. So many deaf children have been taught to speak intelligibly that the statement, "This child will never speak," is not only an unnecessary blow to the poor young father and mother, but a gratuitous insult to hundreds of conscientious teachers of the deaf. And the remark about day schools is more or less fiction.

It is perhaps too much to ask of a busy physician that he inform himself as to the methods used in teaching the deaf; but he need not go so far in the direction of misinformation as to inquire, as two different physicians have inquired of two different mothers of my personal acquaintance, "Has he begun to learn Braille yet?"

Suppose we imagine an ideal interview with an ideal physician who has learned what to say to these stricken mothers. Suppose he should say:

"You must not be too unhappy about this; and you must not imagine that your child will be unhappy all his life because he is deaf. He can become a happy, cheerful, useful individual. He will grow and develop mentally as well as physically, and you will be surprised to find how interesting it will be to watch his development and help it along. You will have to give him a great deal of help, more than the average mother must give her child; but you will have a correspond-

ing reward, and you will be surprised some day to find that getting the better of deafness is an exciting and exhilarating process. You may not believe this now, but it is true.

"You have much to learn, and you must begin right away. Accept the fact of your child's deafness, and don't keep running around trying to find a cure. Instead, find out about schools, find out what you can do for him at home. He must be supplied with occupation, not merely toys to play with, but constructive activities. His education must begin at once, for you can teach him to recognize form and color, and to identify and match objects and pictures; and this is the beginning of language.

"I will tell you where to go for information. Write to the Volta Bureau, 1537 35th Street, N. W., Washington, D. C., for pamphlets on the home training of the small deaf child, and for information about schools and classes for the deaf. Subscribe for the *Volta Review* and read it every month. Learn what other mothers are doing for their deaf children. Write to the John Tracy Clinic, 924 West 37th Street, Los Angeles, Calif, and ask about the correspondence course for mothers of preschool deaf children. Read and think and study and work; and you will find so much to do that you will forget to be unhappy."

Suppose the baby has some hearing. It is never safe to assume that this is not the case until sustained efforts have been made, over a considerable period of time, to utilize any possible hearing that may remain. Does the doctor know how much is being done, in all the most progressive schools for the deaf, to use the hearing of even the smallest children? Does he advise the mother to talk and sing in the child's ear while the child is seated on her lap, or lying beside her, so that the vibration of her voice may be felt? Does he mention talking, close to the child's ear, in front of a mirror, so that the child may watch the mother's mouth in the mirror, and thus make use of sight, touch and hearing simultaneously? This is very important, especially with a young child whose hearing cannot yet be accurately measured.

Does the doctor have an audiometer in his office, to measure and chart the hearing loss of an older child, or an adult? Can he advise about a hearing aid, or can he direct the mother to a center where she may obtain information about hearing aids and experiment with different makes? Is there such a center within a reasonable distance?

There is so much information the doctor could offer! Suppose the patient is a school girl or boy who is just beginning to lose some hearing. Does the doctor know what facilities are available in his community for such children? Are there lip-reading classes in the public schools? Are there periodic hearing tests? Is there a supervisor of special education to decide what this child needs, and what the public school system has to offer? If the child is so deaf that lip reading alone will not enable him to keep up in public school, is there a hearing-aid class available?

Many physicians are still very conservative on the subject of hearing aids. I know a mother who was convinced that her five-year-old girl had considerable hearing, and she went to her otologist to ask about the advisability of a hearing aid.

"Don't think of such a thing," answered the physician. "She is much too young. Besides, it's just a fad. Everybody wants a hearing aid these days. It's just a fad."

Later, an audiometer test by a teacher of the deaf revealed that the little girl had usable hearing in the speech range. She was fitted with a wearable aid — yes, a wearable aid — which she wore at certain periods every day, both at school and at home; and she is rapidly acquiring a hearing vocabulary, which, with her growing lip-reading ability, is making an incalculable difference in her life, and in the lives of her mother and father.

We cannot make general rules about such matters, but it is best to be open-minded and experimental and give every child the benefit of a consistent and sustained effort to use every bit of hearing he may have.

As for adults, the physician also has a definite responsibility to fulfill, and he needs to have a good deal of information on hand to pass along to his patient. If there is a hearing-aid center in the city, what services are offered? Are there sample instruments for the patient to try? Are there lip-reading classes at the center? What other lip-reading facilities, public and private, does the city afford? Where may the patient go for vocational aptitude tests, psychological tests, if these are indicated; and where may he obtain help in getting a job?

For the adult whose hopes the doctor has blasted by announcing, "There is no cure," there are three immediate problems: Communication, social adjustment and a job. Of course, the communication part of it is an important adjunct of social adjustment and of job finding. The individual who has succeeded, by means of lip reading plus a good hearing aid, in educating himself until he can understand easily most of what is said to him, has already largely solved his own problem. Yet he may be afraid of growing more deaf, and he may want to know whether he ought to give up his present means of livelihood and find another.

This, again, may be out of the physician's province — we can't ask him to do everything! — but he could have some reassuring information at hand to give his patient's spirits a boost. He might have a few instances of successful deaf and hard-of-hearing persons to offer besides Beethoven and Edison and Helen Keller. The United States Office of Education once listed over 250 means of earning a living in which deaf and hard-of-hearing persons were engaged; and that was over 10 years ago; there would be a lot more on that list now. The Civil Service Commission has compiled separate data on the deaf and the hard of hearing and the positions open to them under Civil Service. All this information is available in printed form for the doctor's files. In every part of the country, the deaf and hard-of-hearing are successfully engaged in a surprising variety of activities. There are totally deaf young men and women, educated in schools for the deaf, who have gone on to college with the normally hearing,

and have been able to compete with them in impressive situations as chemists, engineers, architects, draftsmen, accountants and what not. School teachers, losing a part of their hearing, have put on hearing aids and continued teaching. College professors have gone on lecturing. United States Senators and Congressmen have gone on legislating, with little black or gray buttons in their ears. Bernard Baruch continued his "office" in Lafayette Park, Washington, D. C., long after he joined the brigade of hearing-aid users. Even Mrs. Roosevelt carries one of these little aids to every important meeting she attends.

These are some of the answers that a physician could have ready when his patient asks the question, "What can a hard-of-hearing person do?" These are a few of the examples he can mention when the patient says, as a patient once said, "Tell me how to go on living, notwithstanding I am deaf." The doctor should be able to say sincerely, from his own knowledge, "If you will educate yourself, you can do almost anything that a person with normal hearing can do."

To sum it all up, the doctor should be able to offer constructive advice to the patient he cannot help medically. He should have at hand concise, accurate and definite information as to what may be done for such a patient, child or adult. He should know where that patient may go for further help. He should know what local and national organizations offer facilities for the hard of hearing and the deaf. The extraordinary demands made on such organizations are indicative of the great need there is for the services they offer; and the physician should do his part in extending cooperation.

Deafness is the most technical of infirmities. It requires expert treatment, whether medical or educational; and only one who understands thoroughly the problems of deafness can deal with them adequately. More than any other person, the physician should understand these problems and know the answers. There is no reason why he should continue to offer his patients a stone when he could give them bread.

John Tracy Clinic.

THE MANAGEMENT OF THE ACUTE EAR.*

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Patients frequently present themselves with the complaint of acute otalgia, or earache, and it behooves the physician to make a differential diagnosis. All cases of otalgia fall into one of several groups: otalgia secondary to pathology of the external ear, otalgia secondary to pathology of the middle ear, and otalgia of referred origin, *i.e.*, pain referred to the ear from distant foci. There is no ordinary sensory nerve supply to the internal ear, hence diseases of the internal ear are unassociated with earache.

All otalgia is secondary to irritation of the sensory nerve endings of the Vth, IXth and Xth cranial nerves. Primarily, the sensory distribution of the auricle and external auditory canal is through the trigeminal (Vth) cranial nerve. The depths of the external ear canal, especially the upper and posterior portions, are supplied by terminals from the vagus (Arnold's nerve). This explains the cough reflex elicited when cleaning cerumen from the depths of the ear canal with a spoon curette or applicator. The tympanic membrane itself is largely supplied by sensory branches of the glossopharyngeal nerve (Jacobson's nerve), though vagal and trigeminal branches are also present. There may also be some sensory branches from the facial nerve through the geniculate ganglion.

It is, therefore, easy to understand that lesions remote from the ear, but within the sensory distribution of the Vth, IXth or Xth cranial nerves, may be associated with otalgia; in fact, in about half the cases complaining of otalgia, no aural pathology is demonstrable, the pain being of referred origin. In the remaining cases, external and middle ear path-

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ology is about equally prevalent. Generally speaking, external otitis is the major offender in the warmer weather, and otitis media is found more often in colder seasons. This is not difficult to explain if we remember that external otitis is associated primarily with pathology of the hair follicles of the skin of the cartilaginous canal, and during the warmer months these glands are more active. In addition, swimming and bathing are in vogue, and furunculosis is common. In colder weather, colds and sinusitis are the order of the day, with acute otitis media as a common complication.

ACUTE EXTERNAL OTITIS.

External otitis, as stated above, is usually manifest as a folliculitis of the hair follicles of the skin over the cartilaginous ear canal. In this case it is spoken of as a *circumscribed external otitis* or *furunculosis*. Occasionally, however, there is a diffuse inflammation, as in a chronic eczema which has become acutely infected, and this is spoken of as a *diffuse otitis externa*. In either event the patient will have acute pain in the ear, which is aggravated by lying on the ear, by palpation over the tragus or by manipulation of the auricle, but there is no appreciable hearing loss (not over 10 db. usually). Otoscopic examination will usually reveal the pathology quite readily.

The conservative management of these cases is to be preferred. Continuous hot, wet dressings serve to relieve the discomfort and delimit the pathology. Recently, the author has employed a new technique which has proven of definite value. A sterile gauze tip or a runner of ¼-inch plain sterile gauze tape is moistened with Otosmosan* and this is packed into the canal rather tightly. Dry heat is applied over the ear and Otosmosan is added to the gauze every two or three hours by the patient to keep the gauze saturated. This method has served several useful purposes: the glycerine base of the Otosmosan serves as a continuous wet dressing and at the same time is dehydrating, while the sulfathiazole

*Otosmosan is a mixture of 20 per cent sulfathiazole and urea in absolute glycerine, and is marketed by the Doho Chemical Corp.

acts as an antiseptic and prevents the spread of the infection to other hair follicles.

If the furuncles point, incision is carried out and the Otosmosan packing is reinserted. Furuncles which do not point are never incised, for to do so will spread the infection and may lead to a widespread cellulitis or chondritis. Some otologists routinely expose the ear to ultraviolet or deep X-ray therapy, as this tends to localize the infection and reduce the pain somewhat. It may be necessary to prescribe codeine and aspirin for pain, and occasionally morphine may be required.

Following the amelioration of the acute process, the author routinely prescribes an ointment containing 3 per cent of ammoniated mercury, for daily use by the patient for at least a week, to insure against a recurrence. It is important to warn the patient against permitting water to stagnate in the ear canals and to impress upon him the advisability of having the ears properly cleaned by a physician every four to six months if recurrences are to be prevented.

ACUTE OTITIS MEDIA.

The management of acute otitis media varies according to whether the tympanic membrane is still intact or already perforated and discharging. Before the drum has either ruptured or been incised, the physician must decide whether myringotomy is indicated, and all other measures will be dictated by the first decision.

The author feels that every effort should be made to clear up the pathology without myringotomy, but that if in doubt, it is far better to err on the side of a myringotomy properly performed than endanger the patient with a spontaneous rupture of the eardrum. (Spontaneous perforations are almost always near the center of the drum and are seldom adequate in size for proper drainage.) If one believes that he can procrastinate for a while, hygroscopic ear drops (such as Auralgan) may be prescribed, but under no circumstances should a preparation containing phenol or other caustics be prescribed. No possible benefit can be expected from phenol

applied topically. The therapeutic virtue of practically all ear drops lies in the dubious ability of their glycerine base to remove fluid from the middle ear by osmosis through the drum membrane. Further, phenol will produce a superficial escharosis and hyperemia of the drum and thus obscure all the landmarks, so that next day the physician will be more confused than ever as to further procedure.

If one decides on the use of a hygroscopic ear drop for a few hours or over night, he should choose the most hygroscopic glycerine available and one that is as concentrated as possible, *i.e.*, it should contain as few other ingredients as possible and *absolutely no water*. For this purpose, the author prefers Auralgan to all other commercially available preparations. (The only exception to this rule is in *myringitis bullosa*, where a sulfonamide-glycerine ear drop is preferable to sterilize the canal after the vesicles have ruptured.)

It is imperative that adequate chemotherapy be given either orally or parenterally. In these cases, combined sufonamide and penicillin is superior to either alone, and sulfonamide has proven more efficacious than penicillin, if it is decided to use but one.

Particular attention should be paid to the nasopharynx since practically every case of middle ear infection is secondary to pathology of the nasopharynx. In adults, careful vasoconstriction and local chemotherapy is carried out by nasal atomizer sprays. The patient is instructed to blow his nose with great care, being always sure to blow both sides at once and with both nostrils held loosely. To do otherwise will cause nasal secretion to be blown into the Eustachian tubes and will aggravate the ear pathology. After cleansing of the nasopharynx by capillary suction or irrigation, Eustachian inflation may be tried and often serves to clear up the middle ear pathology promptly. In other instances such inflations have precipitated a fulminating otitis media in a few hours' time, so that the author always warns the patient that the treatment may clear up the ear condition or it may precipitate an ear abscess which will quickly need myringotomy. In

children, Eustachian inflations are usually not feasible but careful attention should still be paid to the nasopharynx and to the matter of proper blowing of the nose.

If the patient does not respond to the above-outlined conservative treatment, or if his condition grows worse, then a carefully performed myringotomy should be carried out. In children over two years of age and in nervous or uncooperative adults, general anesthesia is preferred; otherwise the patient may be frightened to the point of not permitting proper after-care. The author prefers a curvilinear incision in the lower posterior quadrants, since this will provide dependent drainage whether the patient is lying on his back or is in the erect position.

If the tympanic membrane has already ruptured spontaneously when first seen by the otologist, he must determine the adequacy of the drainage. Most spontaneous perforations are neither adequate in size nor located in a position of dependency. In either instance, an elective myringotomy should be performed in spite of the spontaneous perforation. Such an incision will serve to provide adequate drainage for the middle ear and allow the spontaneous perforation to close by rapid healing. The greatest danger of spontaneous perforation is its tendency towards permanency. This is aided by the prolonged duration of the discharge through the inadequate perforation and the ever-present tendency of the edges to retract with subsequent enlargement of the perforation.

Following such myringotomy, *all local glycerine medication should be discontinued.* To place glycerine, a foreign chemical substance which is not absorbed by the mucous membrane, into an already diseased middle ear is to add insult to injury. It simply increases the work of an already diseased part.

The recommended after-care of a surgically incised eardrum will vary with different otologists. Some prefer the "wet treatment" (frequent irrigations) and others prefer the "dry treatment" (no irrigations). In the experience of the author, the dry treatment or a modification thereof is preferable in most cases. Consequently, unless the amount of discharge evacuated from the middle ear by myringotomy is copious, a pledget of sterile cotton should be placed in the canal

and the patient or parent instructed to change this as often as necessary. The patient should be seen next morning, or at least within 24 hours, in every case. In many cases the ear will be found dry and the drum healed, since no bacteria from the external canal has been irrigated into the middle ear, and the evacuation of the serous or serosanguineous exudate has permitted the middle ear to recover. In these cases, no further treatment is necessary and no permanent evidence of the myringotomy will remain.

In other cases a fair amount of discharge is found in the ear canal next day. This should be wiped away, and capillary suction should be applied to evacuate all secretion from the middle ear. If the drum appears to pulsate after thorough cleansing of the canal, there is still secretion under pressure in the middle ear and mass suction should be applied to the external auditory meatus up to three inches of negative pressure (but no higher, for fear of dislocating the ossicular chain). Capillary suction alternated with mass suction should be carried out until the middle ear is dry. A sterile pledget of cotton is again inserted in the canal and the patient is seen in 24 hours. Meanwhile, chemotherapy should be administered orally and/or parenterally, and the patient should be placed at absolute rest.

If the discharge is copious and tenacious, an occasional irrigation of the ear with *sterile* normal saline solution may be ordered. Boric acid solution should not be used as there is no rationale for its use and there are several serious objections to it. Boric acid solutions have no bactericidal properties. Furthermore, saturated solutions vary in strength but are all hypertonic, not isotonic. (Solutions as prepared by the patient with boiling or hot water may contain as much as 20 per cent of boric acid; as prepared by a pharmacist, the usual solution will contain approximately 5 per cent boric acid. To be isotonic, the solution must contain 1.7 per cent boric acid.) The surface tension of an aqueous solution of boric acid is quite high so that it has no detergent or cleansing properties; in fact, such a solution will not mix well with secretions and hence may actually "pack in" the secretion rather than remove it from the ear canal.

In addition to these objections, most solutions of boric acid as prepared in the home or in the hospital ward are supersaturated when made, since they are made by heat. As soon as this solution comes in contact with the ear canal and becomes cooled, some of the boric acid precipitates out as whitish coating over the eardrum and canal, thus further obscuring the landmarks. Whereas normal saline solution has no antiseptic properties *per se*, it is at least cleansing, nonirritating and isotonic. If an antiseptic is desired, a 1-10,000 aqueous solution of zephiran chloride* is recommended, since it is not only germicidal but has a very low surface tension and hence exhibits great cleansing properties. It is also nonirritating to tissues, not containing a heavy metal or phenol in its formula.

If irrigations become necessary to clear the ear canal of tenacious secretion and permit drainage for the middle ear, they should be used as infrequently as possible and discontinued as quickly as possible, since the continuous bathing of the parts with water will produce edema and maceration of the tissues and prolong the pathologic process. It is imperative to clear up the discharge as quickly as possible and permit the perforation to heal, if we would avoid a permanent perforation and hearing loss.

REFERRED OTALGIA.

As has been mentioned above, otalgia may result from referred irritation of the Vth, IXth or Xth cranial nerves. The obvious implications of this statement are that pathology from many and varied organs and tissues may result in otalgia.

Dental pathology accounts for a large percentage of the referred pain in the ear. Dental caries, especially of the molars, frequently are attended by otalgia, even before severe toothache occurs. Impacted wisdom teeth, especially of the upper jaw, frequently are the cause of earache. Obstruction of a salivary gland duct by stone or other pathology of the salivary glands may lead to otalgia, as well as ulcerations of

*Zephiran chloride is a mixture of alkyl-dimethylbenzyl ammonium chlorides, and is marketed by the Winthrop Chemical Co.

the buccal or gingival oral mucosa; such otalgia is, of course, of trigeminal origin.

Pharyngeal pathology is also frequently attended by earache. A common complaint in peritonsillar abscess is earache on the affected side. Occasionally an acute tonsillitis will have similar associated otalgia. This is usually due to irritation of the branch of the glossopharyngeal nerve which traverses the fascia of the tonsillar fossa on its way to the ear. This also accounts for the frequent occurrence of earache following tonsillectomy, as in many of these cases the nerve is exposed during the operation and becomes subsequently engulfed in scar. Occasionally an acute edema of the soft palate or uvula will be associated with otalgia for much the same reason. Conversely, the author has, on several occasions, made use of this anatomical fact in the removal of a foreign body from against the eardrum in an adult where previous attempts had been unsuccessful and the patient was hurt. Injection of a few drops of novocaine back of the tonsil usually will relieve the pain of manipulation against the eardrum. In fact, sometimes the same thing may be accomplished by spraying the throat on the same side thoroughly with 2 per cent pontocaine solution.

Otalgia of vagal origin, though not so commonly encountered as that from trigeminal or glossopharyngeal irritation, nonetheless, is of not rare occurrence. One of the cardinal symptoms of tuberculous ulceration of the larynx is hoarseness with pain in the ear, usually referred to the tip of the lobule and lancinating in character. Other laryngeal pathology will also produce otalgia when the superior laryngeal nerve is involved. The obvious management of all cases of referred otalgia is to find the causative pathology and correct it. The pain in the ear will subside almost immediately after the elimination of its cause. No local therapy to the ear is necessary in any of these cases and none should be carried out. Occasionally it may be necessary to prescribe sedatives or analgesics for the immediate relief of the pain during other forms of treatment.

1205 St. Paul Street.

REPORT OF A DEATH FROM PONTOCAINE HYDROCHLORIDE.

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In recent years pontocaine hydrochloride has begun to replace cocaine for topical analgesia in otolaryngology. This tendency may increase as it becomes recognized that pontocaine is equally or more effective and less toxic than cocaine in the concentrations that are used. According to Wood and Osol[1] pontocaine has 15 times the anesthetic power of cocaine, but is two and one-half times as toxic in the same concentration; however, a 2 per cent solution of pontocaine is the concentration of choice and is three times as strong and one-half as toxic as a 10 per cent solution of cocaine. Pontocaine does not have the vasoconstrictor effect of cocaine, but this can be produced by adding epinephrine to the pontocaine solution.

The toxic reactions of pontocaine are similar to those of cocaine and other local anesthetics. These are well known and will not be discussed.

Although the dangers of cocaine are well known, reports are just beginning to appear in the American literature concerning the dangers of pontocaine. Because of this, many laryngologists may believe that the use of this drug is without danger; however, recently there have been several severe reactions to local anesthetics at this hospital, with two fatalities. I was present when one death occurred, and I believe the case is worth reporting to show how such a reaction may occur suddenly and without warning.

CASE REPORT.

Mrs. R. F., a 27-year-old housewife, was admitted to the hospital on Feb. 5, 1945, for a diagnostic bronchoscopy. For four years she had had recurrent attacks of left posterior chest pain and hemoptysis with

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increasing severity and frequency. Visits to numerous physicians had been made without a definite diagnosis being established. Chest X-rays, including bronchography, done elsewhere, were reported as negative. Sputum was negative for acid-fast bacilli. No other complaints were offered. The family history was also noncontributory except for a possible unknown type of allergy in her father. No history was obtained of previous use of local anesthetics except when the first bronchogram was done. It was not known what drug was used at that time. The physical examination and laboratory findings were unremarkable on admission.

On Feb. 6, 1945, the patient was bronchoscoped and a normal tracheobronchial tree was described. The preoperative medication consisted of nembutal 0.1 gm., two hours before bronchoscopy, and morphine 0.01 gm., with scopolamine 0.4 mg., one-half hour preoperatively. Topical analgesia to the mouth, pharynx and trachea was carried out, using in all about 5.0 cc. of a 2 per cent solution of pontocaine. No abnormal effects occurred, and the patient was discharged in good condition the next day.

On Feb. 16, 1945, the patient reported to the clinic for a bronchogram. At 1:30 P.M., she received barbital 0.4 gm., by mouth. Forty-five minutes later, topical analgesia was started in preparation for the bronchogram. A 2 per cent solution of pontocaine was used for this, a short spray of the solution being directed into the nose and pharynx. After an interval of about four minutes 2 cc. of the solution was instilled into the trachea. A considerable amount of this was coughed out. Four minutes later, a rubber catheter was passed through the nose into the trachea. As the cough reflex was not completely abolished, an additional 2 cc. of the solution was put into the trachea through the catheter. Immediately afterward the patient complained of dizziness and an excess of secretions seemed to accumulate in the trachea. All secretions were at once aspirated through the intratracheal tube and the latter removed. The patient appeared pale and cold and would not respond to questions. The pulse was weak and thready, but before the rate could be determined she had a sudden generalized clonic convulsion of short duration. Intravenous sodium phenobarbital 0.065 gm., the only barbiturate quickly available, was immediately given, but five similar convulsions followed. No pulse, respiration or blood pressure could be determined after the first convulsion. Artificial respiration, a carbon-dioxide and oxygen mixture by mask, intravenous coramine and intracardiac epinephrine were of no avail. Death was pronounced at 2:45 P.M.

Although no autopsy was obtained, the death was typical of those due to local anesthetics and this case can be classified as one due to pontocaine.

DISCUSSION.

This case is particularly interesting because the patient had had topical pontocaine anesthesia without incident 10 days prior to the time the same procedure resulted in her death. Thomas and Fenton,[2] Derbes and Engelhardt,[3] and Phillips and Congleton[4] have all reported pontocaine reactions, some of which were fatal. I can find no reported case with a history similar to the one just described; however,

several of the cases reported by Thomas and Fenton had had previous injections of procaine for teeth extractions. It was suggested that the procaine had sensitized those cases to substances with a similar chemical formula. That may be the explanation for those reactions as procaine and pontocaine are chemically closely related. This has been shown to be possible by Rothman, Orland and Flesch[5] in their work on skin sensitivity to the various local anesthetics. My case had a 10-day period between receiving the two doses of pontocaine, and in this time she may have developed a sensitivity resulting in the fatal reaction after the second application of the drug. Consideration of this possibility must not be neglected as many patients receive multiple topical anesthetics for repeated endoscopy. The possibility of such accidents must be remembered every time a topical anesthetic is given, even if the same procedure has been done before. It is unfortunate that there is no known test which will reveal such a sensitivity. It is known, however, that reactions occur more often in allergic persons than in the nonallergic. Asthmatics are frequently very sensitive to pontocaine, and the use of a small amount of the drug may bring on an acute attack of asthma.

Another possible explanation for the fatal reaction in my case is the amount of sedation that was used. The amount the patient received for the first procedure may have been sufficient to counteract the central nervous system effect of the pontocaine while the relatively small amount of sedation during the second procedure would not do so. (First procedure, nembutal 0.1 gm., morphine 0.01 gm., scopolamine 0.4 mg.; second procedure, barbital 0.4 gm.)

It is also possible that the patient may have aspirated the pontocaine into the pulmonary alveoli during the second procedure causing rapid absorption of the drug, resulting in a large amount suddenly reaching the central nervous system causing the reaction.

Still another explanation is the possibility that the solution that was used during the second procedure may have been

stronger than 2 per cent, with the patient receiving more pontocaine than desired. This was found to be true. A rough analysis of the solution showed no impurities but did reveal that it was about a 6 per cent solution. The explanation for this is that the solution was in a poorly stoppered bottle and had concentrated itself by evaporation.

In all probabilities it was a combination of several or all of these factors that caused the fatal reaction.

CONCLUSION.

This case report of a death following the topical application of pontocaine may help to show the dangers associated with the use of that drug. As it is not possible to tell in advance which patient may be sensitive to this drug, all possible care must be carried out to avoid such reactions.

REFERENCES.

1. Wood, H. C., and Osol, A.: United States Dispensary, Part II, 1326, 1943.

2. Thomas, J. W., and Fenton, M. M.: Fatalities and Constitutional Reactions Following the Use of Pontocaine. *Jour. Allergy*, 14:145-159, Jan., 1943.

3. Derbes, V. J., and Engelhardt, H. T.: Deaths Following the Use of Local Anesthetics in Transcricoid Therapy. *Jour. Lab. and Clin. Med.*, 22:478-482, May, 1944.

4. Phillips, F. J., and Congleton, V. I.: Pontocaine HCl Reaction Relieved by Dial. *Anes. and Anal.*, 20:233-234, 1941.

5. Rothman, S.; Orland, D. D. S., and Flesch, P.: Group Specificity of Epidermal Allergy to Procaine in Man. *Jour. Invest. Dermatol.*, 6:191-199, June, 1945.

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